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FILE COVERS 1907 - 28 Sep 2005  VOL 143 ISS 14
FILE LAST UPDATED: 27 Sep 2005  (20050927/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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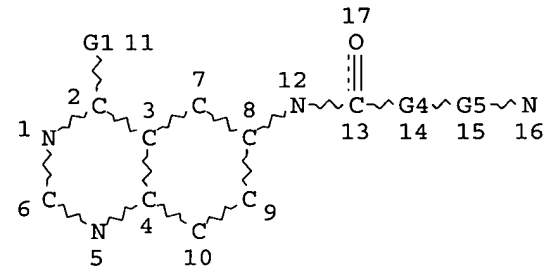

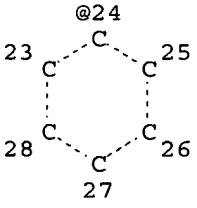

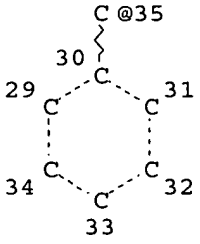

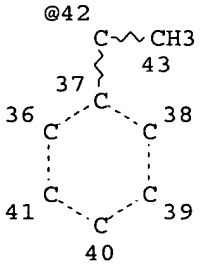

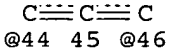

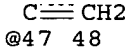

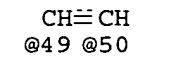

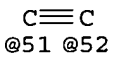

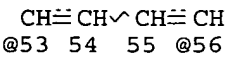


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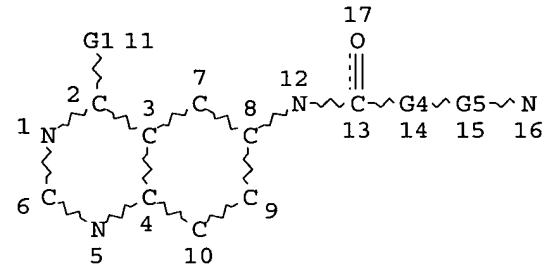

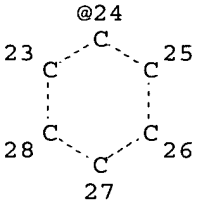

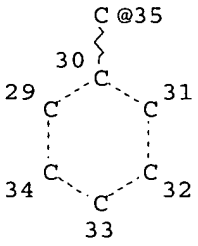

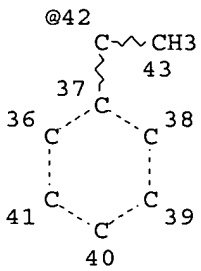

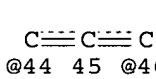

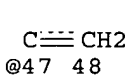

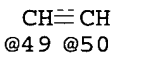

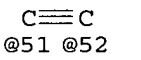

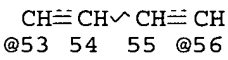

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VAR G4=44-13 46-15/47/49-13 50-15/51-13 52-15/53-13 56-15/C
REP G5=(1-9) C
NODE ATTRIBUTES:
NSPEC IS C AT 16
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE
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L8 ANSWER 1 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:638739 HCAPLUS
DOCUMENT NUMBER: 143:159556
TITLE: Novel pharmaceutical combinations containing scopine or tropic acid esters and EGfR-kinase inhibitors
INVENTOR(S): Pieper, Michael P.; Pohl, Gerald; Jung, Birgit; Pairet, Michel
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005065687	A1	20050721	WO 2005-EP9	20050104
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US 2005203088	A1	20050915	US 2005-28268	20050103
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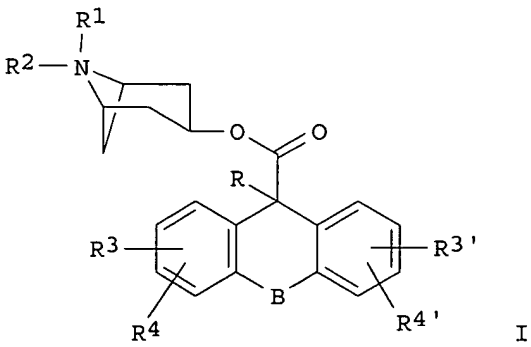

I

AB The invention relates to novel pharmaceutical compns. based on compds. of general formula (I) wherein X and the groups A, B, R, R1, R2, R3, R3', R4 and R4' have the designations cited in the claims and in the description,

and EGFR-kinase inhibitors. The invention also relates to methods for the production of said compns., and to the use of the same for the treatment of respiratory illnesses. Thus an inhalation powder contained (μg/capsule): scopine or tropic acid ester 60; 4-[(3-Chloro-4-fluorophenyl)amino]-6-[2-((S)-6-methyl-2-oxomorpholine-4-yl)ethoxy]-7-methoxyquinazoline 3500; lactose 3440.

IT **314771-10-3 439081-11-5 439081-12-6**
439081-13-7 439081-14-8 439081-17-1
439081-18-2 439081-24-0 439081-26-2
439081-30-8 439081-39-7 439081-40-0
439081-48-8 573649-57-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combinations containing scopine or tropic acid esters and EGfR-kinase inhibitors)

RN 314771-10-3 HCAPLUS
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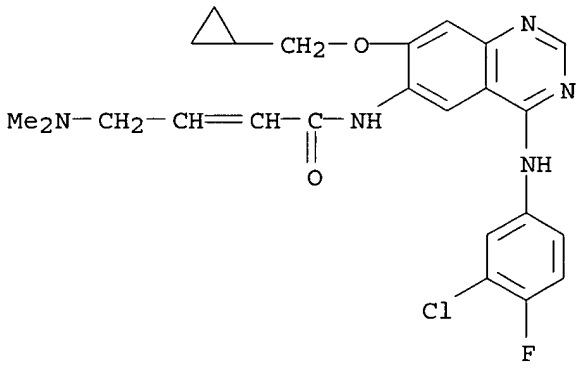

RN 439081-11-5 HCAPLUS
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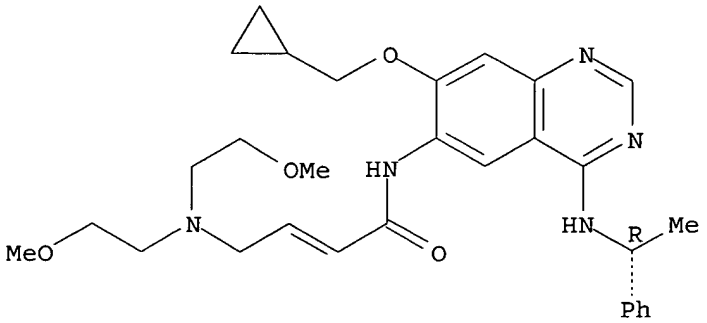
Absolute stereochemistry.
Double bond geometry unknown.



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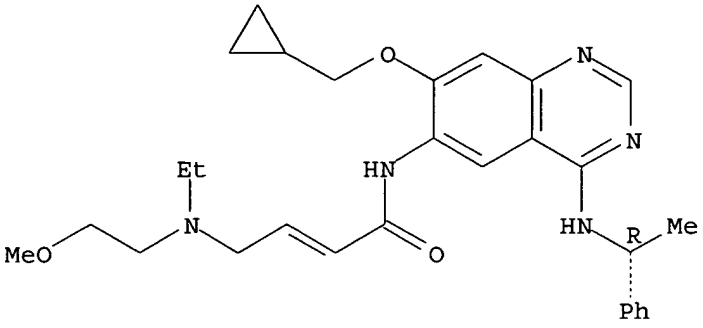
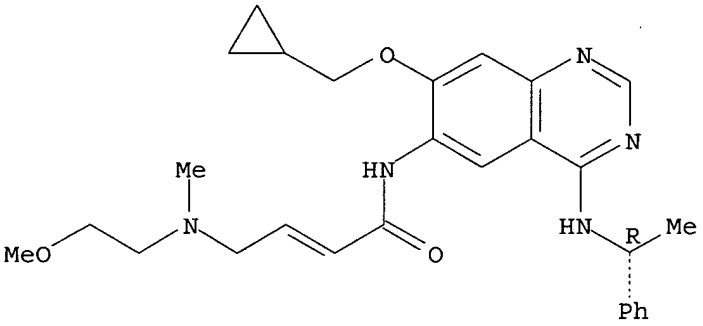
Absolute stereochemistry.

Double bond geometry unknown.



RN 439081-13-7 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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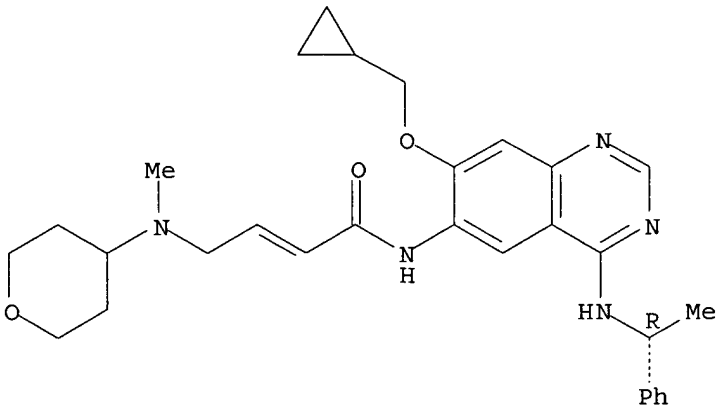
Absolute stereochemistry.
Double bond geometry unknown.



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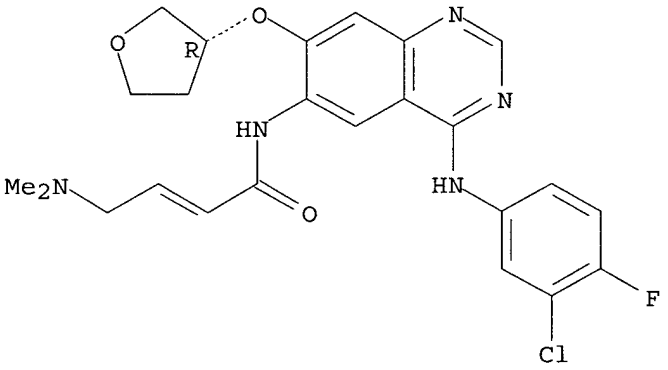
Absolute stereochemistry.
Double bond geometry unknown.



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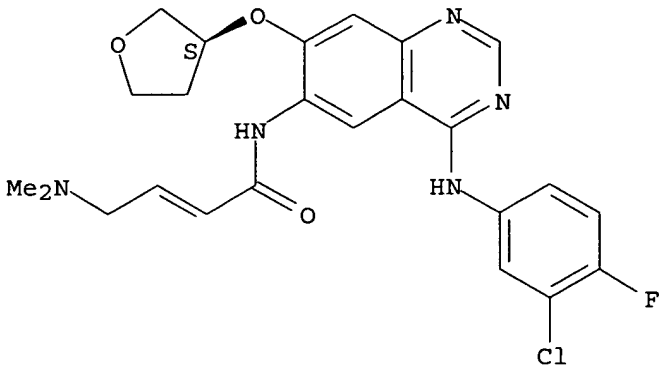
Absolute stereochemistry.
Double bond geometry unknown.



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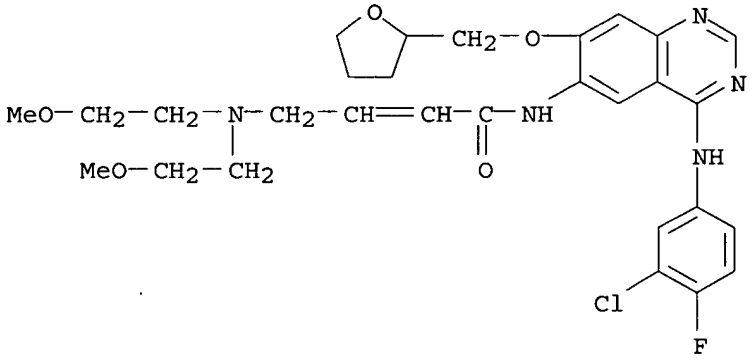

RN 439081-26-2 HCAPLUS
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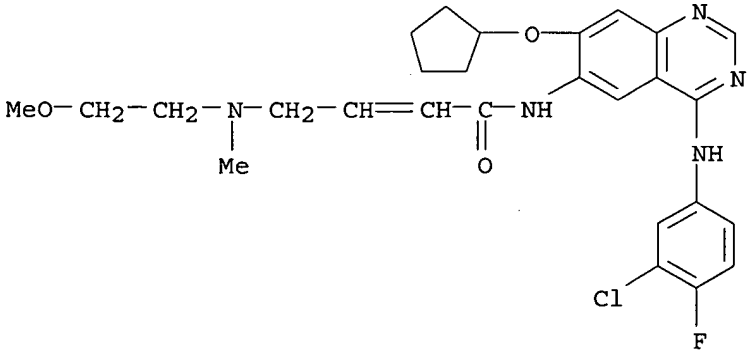

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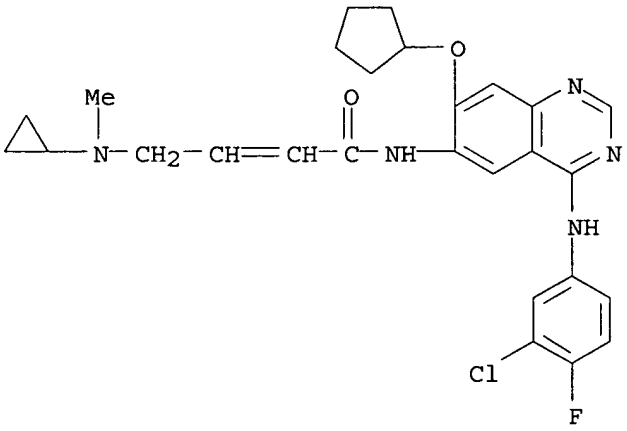

RN 439081-39-7 HCAPLUS
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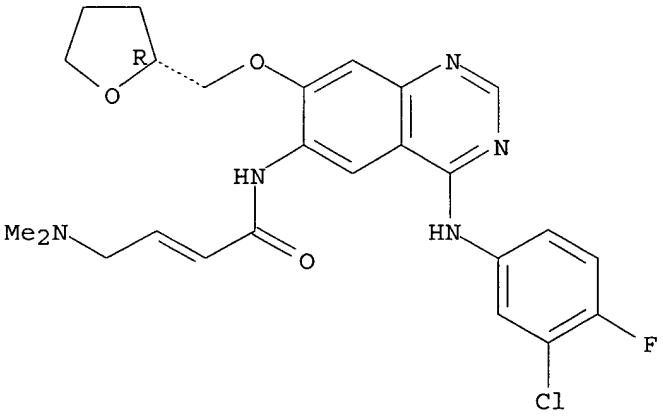
Absolute stereochemistry.
Double bond geometry unknown.



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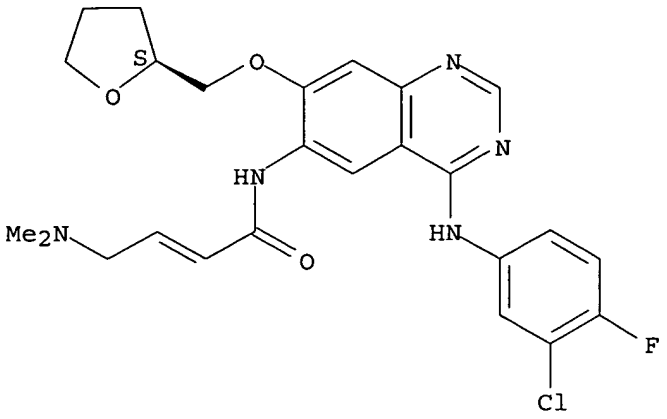
Absolute stereochemistry.
Double bond geometry unknown.



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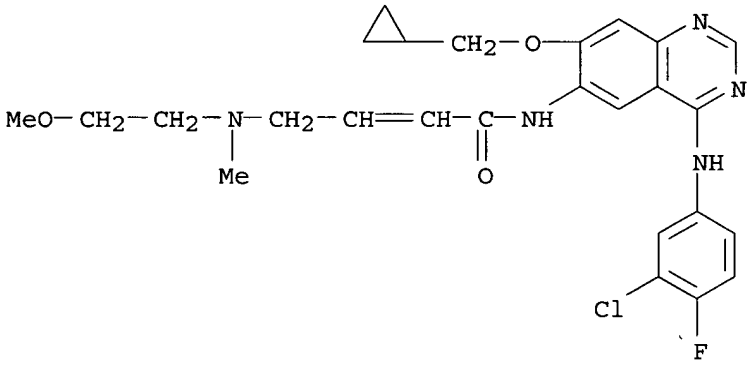

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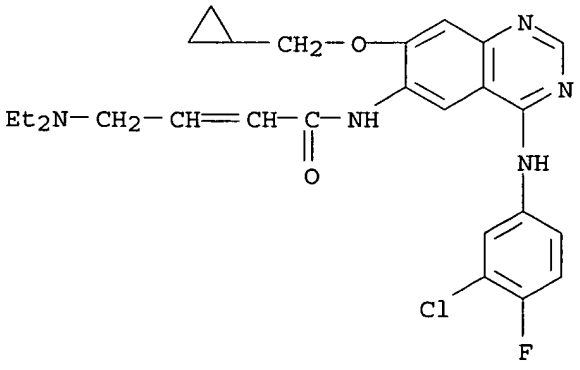
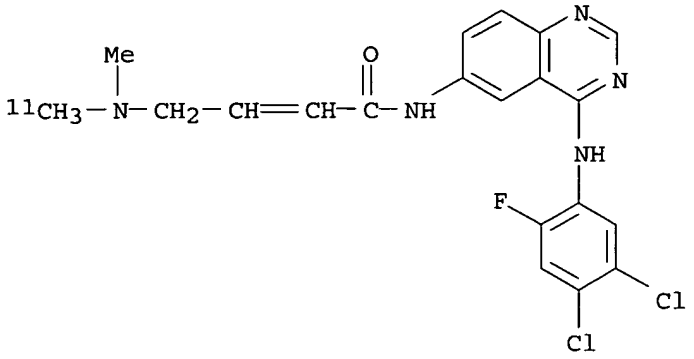


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

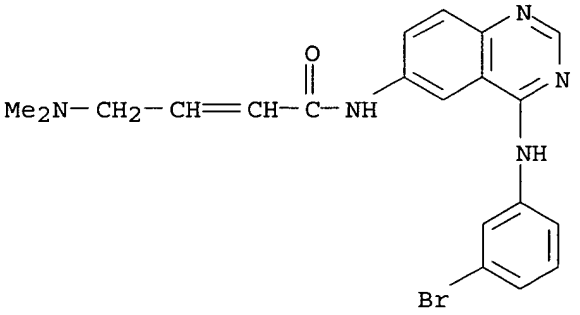
L8 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:601190 HCAPLUS
DOCUMENT NUMBER: 143:244173
TITLE: High-Affinity Epidermal Growth Factor Receptor (EGFR) Irreversible Inhibitors with Diminished Chemical Reactivities as Positron Emission Tomography (PET)-Imaging Agent Candidates of EGFR Overexpressing Tumors
AUTHOR(S): Mishani, Eyal; Abourbeh, Galith; Jacobson, Orit; Dissoki, Samar; Daniel, Revital Ben; Rozen, Yulia; Shaul, Mazal; Levitzki, Alexander
CORPORATE SOURCE: Department of Medical Biophysics and Nuclear Medicine, Hadassah Hebrew University, Jerusalem, 91120, Israel
SOURCE: Journal of Medicinal Chemistry (2005), 48(16), 5337-5348
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies with the anilinoquinazoline epidermal growth factor receptor (EGFR) irreversible inhibitor [11C]-ML03 demonstrated a rapid metabolism of the tracer, which led to its low in vivo accumulation in EGFR overexpressing tumors. To enhance tumor uptake, the chemical structure of the compound was modified, and four new groups of EGFR inhibitors with a wide range of chemical reactivities were synthesized. Chemical reactivity assay of the compds., performed with reduced glutathione (GSH), revealed that the group C (4-(dimethylamino)-but-2-enoic amide) derivative was the least chemical reactive against the nucleophilic attack of GSH. Nonetheless, it demonstrated a high inhibitory potency and bound irreversibly to the EGFR. Consequently, the blood stability of the group C compound (5a, ML04) labeled with 11C was studied. In a time frame of 60 min, no radioactive metabolites were detected in blood. The stability of [11C]-5a, as indicated both from in vitro blood-stability assays and injection into nude rats, was significantly higher as compared to [11C]-ML03. Since group C presented a greater promise for tumor accumulation, it represents, to date, the most suitable candidate for radiolabeling with long-lived positron emission tomog. (PET) radioisotopes.

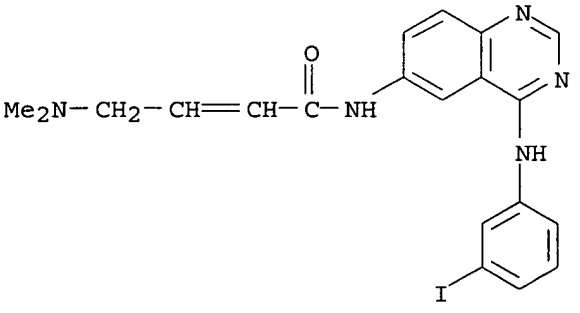
IT **848006-08-6P**
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(11C-labeled anilinoquinazoline EGFR inhibitors: preparation as PET tumor imaging agents)
RN 848006-08-6 HCAPLUS
CN 2-Butenamide, N-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-quinazolinyl]-4-(methylmethyl-11C-amino)- (9CI) (CA INDEX NAME)



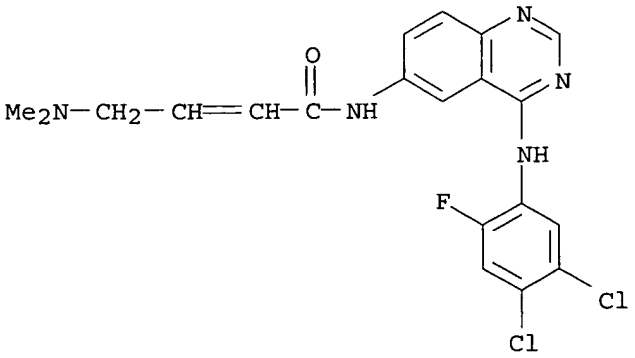
IT **220699-51-4P 746673-21-2P 848006-05-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(11C-labeled anilinoquinazoline EGFR inhibitors: preparation as PET tumor imaging agents)
RN 220699-51-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 746673-21-2 HCAPLUS
CN 2-Butenamide, 4-(dimethylamino)-N-[4-[(3-iodophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 848006-05-3 HCAPLUS
CN 2-Butenamide, N-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:586215 HCAPLUS
DOCUMENT NUMBER: 143:120526
TITLE: Pharmaceutical compositions based on anticholinergics and additional active ingredients
INVENTOR(S): Pairet, Michel; Pieper, Michael P.; Meade, Christopher John Montague; Reichl, Richard; Schmelzer, Christel; Jung, Birgit
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany
SOURCE: U.S. Pat. Appl. Publ., 50 pp., Cont.-in-part of U.S. Ser. No. 824,391.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005148562	A1	20050707	US 2004-6940	20041208
DE 10062712	A1	20020620	DE 2000-10062712	20001215
DE 10063957	A1	20020627	DE 2000-10063957	20001220
DE 10110772	A1	20020912	DE 2001-10110772	20010307
DE 10111058	A1	20020912	DE 2001-10111058	20010308
DE 10113366	A1	20020926	DE 2001-10113366	20010320
DE 10138272	A1	20030227	DE 2001-10138272	20010810
US 2002151541	A1	20021017	US 2001-7182	20011019
US 2002183292	A1	20021205	US 2001-86145	20011019
US 2002137764	A1	20020926	US 2001-40196	20011025
US 2002122773	A1	20020905	US 2001-27662	20011220
DE 10206505	A1	20030828	DE 2002-10206505	20020216
US 2002169181	A1	20021114	US 2002-92116	20020306
US 6620438	B2	20030916		
US 2002193393	A1	20021219	US 2002-93240	20020307
US 2002183347	A1	20021205	US 2002-100659	20020318
US 6608054	B2	20030819		
US 2003158196	A1	20030821	US 2003-360064	20030207
US 2003181478	A1	20030925	US 2003-395777	20030324
US 6890517	B2	20050510		
US 2003203925	A1	20031030	US 2003-413065	20030414

US 2003212075	A1	20031113	US 2003-419358	20030421
US 6696042	B2	20040224		
US 2004024007	A1	20040205	US 2003-613783	20030703
US 2004151770	A1	20040805	US 2004-763894	20040123
US 2004161386	A1	20040819	US 2004-775901	20040210
US 2004176338	A1	20040909	US 2004-776757	20040211
US 2004192675	A1	20040930	US 2004-824391	20040414
US 2005147564	A1	20050707	US 2005-68134	20050228

PRIORITY APPLN. INFO.:

DE 2000-10054042	A	20001031
US 2000-253613P	P	20001128
DE 2000-10062712	A	20001215
DE 2000-10063957	A	20001220
US 2000-257220P	P	20001221
US 2000-257221P	P	20001221
DE 2001-10110772	A	20010307
DE 2001-10111058	A	20010308
DE 2001-10113366	A	20010320
US 2001-281653P	P	20010405
US 2001-281857P	P	20010405
US 2001-281874P	P	20010405
DE 2001-10138272	A	20010810
US 2001-314599P	P	20010824
US 2001-7182	B1	20011019
US 2001-86145	B1	20011019
US 2001-27662	B1	20011220
DE 2002-10206505	A	20020216
US 2002-92116	A1	20020306
US 2002-93240	B1	20020307
US 2002-100659	A1	20020318
US 2002-369213P	P	20020401
US 2003-360064	A2	20030207
US 2003-413065	B2	20030414
US 2003-419358	A1	20030421
US 2003-613783	A2	20030703
US 2004-763894	A2	20040123
US 2004-775901	A2	20040210
US 2004-776757	A2	20040211
US 2004-824391	A2	20040414
US 2001-40196	B1	20011025
US 2003-395777	A1	20030324

AB A pharmaceutical composition comprising an anticholinergic and at least one addnl. active ingredient selected from among corticosteroids, dopamine agonists, PDE-IV inhibitors, NK1-antagonists, endothelin antagonists, antihistamines, and EGFR-kinase inhibitors, processes for preparing them and their use in the treatment of respiratory diseases. Among a number of compds. prepared was N-[2-[3,5-bis(trifluoromethyl)phenyl]ethyl]-2-[4-[(3-hydroxypropyl)methylamino]piperidin-1-yl]-N-methyl-2-phenylacetamide. Inhalable powders include a formulation containing tiotropium bromide, budesonide, and lactose.

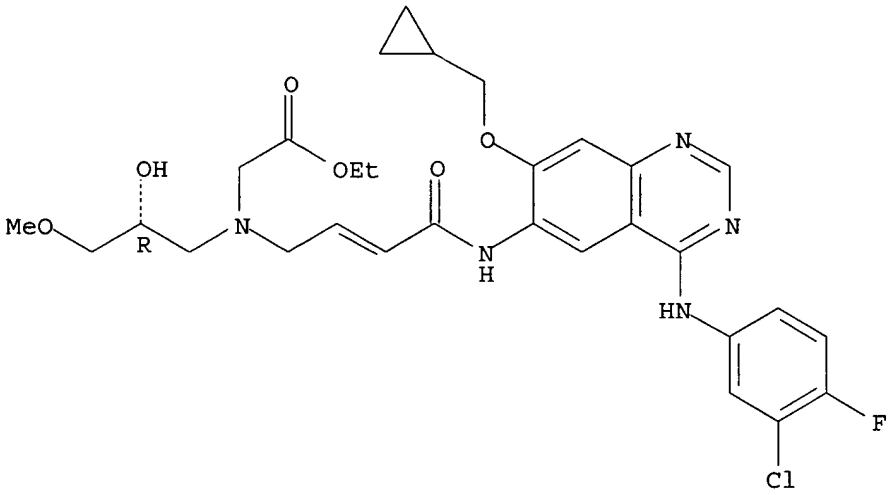
IT **402569-87-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pharmaceutical compns. based on anticholinergics and addnl. active ingredients)

RN 402569-87-3 HCAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

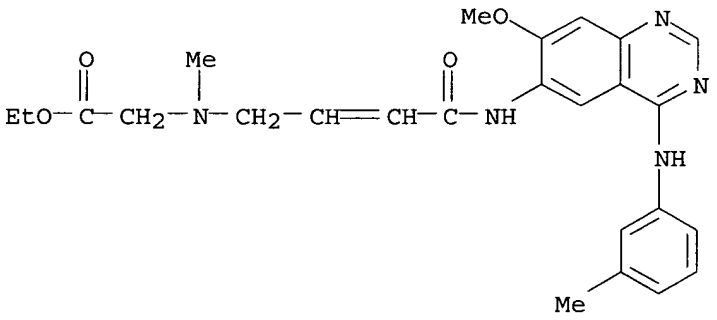
Double bond geometry unknown.



IT **290301-86-9P 290302-19-1P 314771-10-3P**
439081-11-5P 439081-12-6P 439081-13-7P
439081-14-8P 439081-17-1P 439081-18-2P
439081-26-2P 439081-30-8P 439081-39-7P
439081-40-0P 439081-48-8P 573649-57-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. based on anticholinergics and addnl. active ingredients)

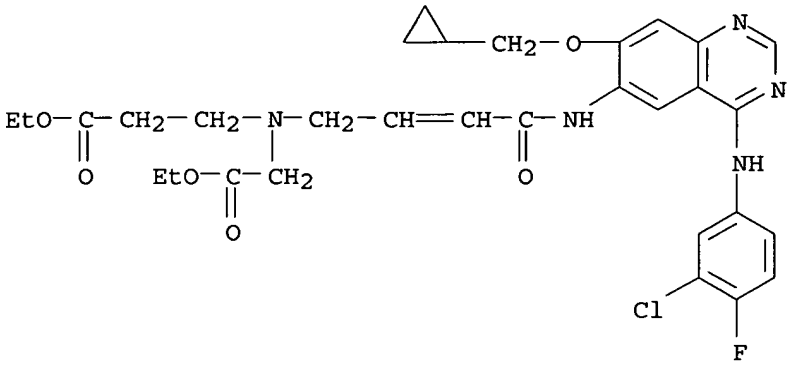
RN 290301-86-9 HCAPLUS

CN Glycine, N-[4-[[7-methoxy-4-[(3-methylphenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

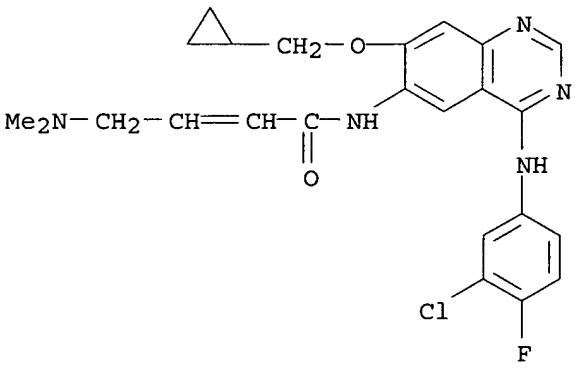


RN 290302-19-1 HCAPLUS

CN β-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

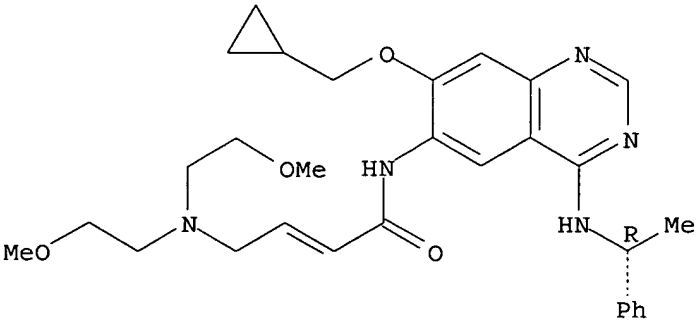


RN 314771-10-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



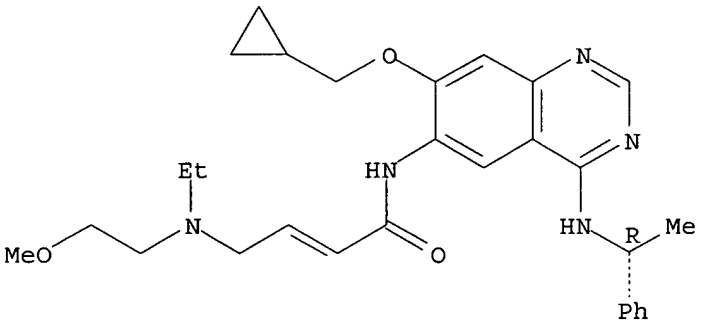
RN 439081-11-5 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



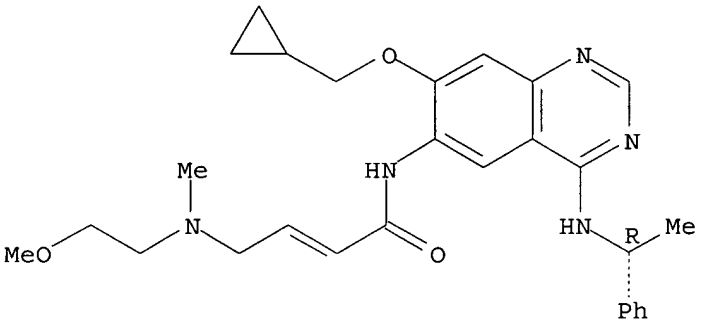
RN 439081-12-6 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



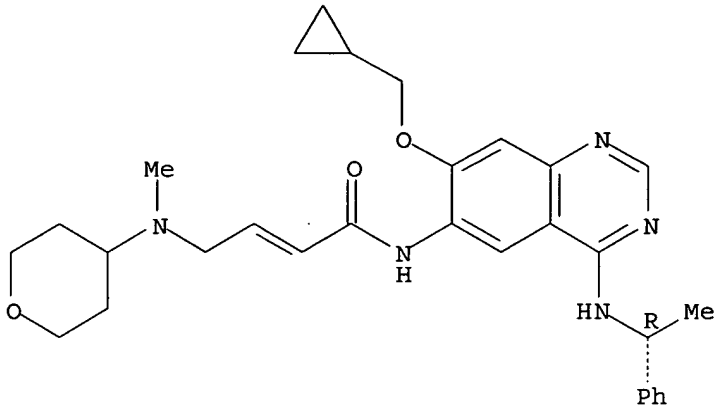
RN 439081-13-7 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



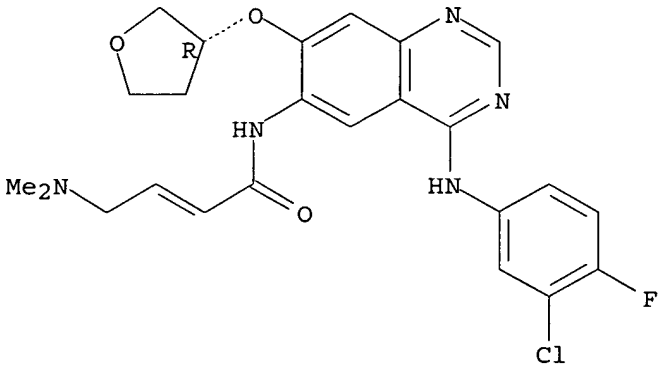
RN 439081-14-8 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



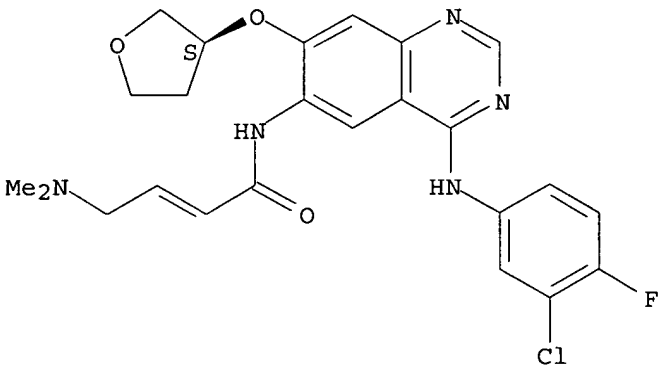
RN 439081-17-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

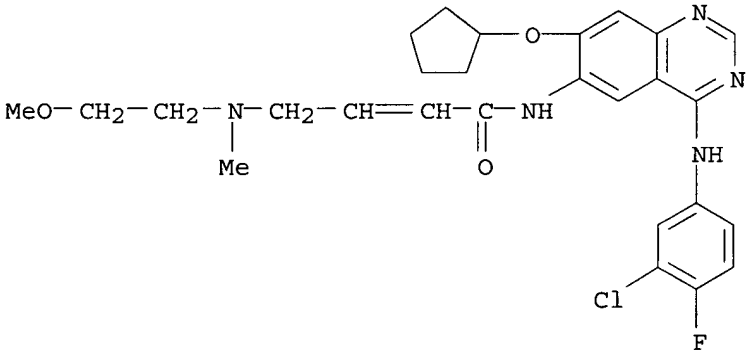


RN 439081-18-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

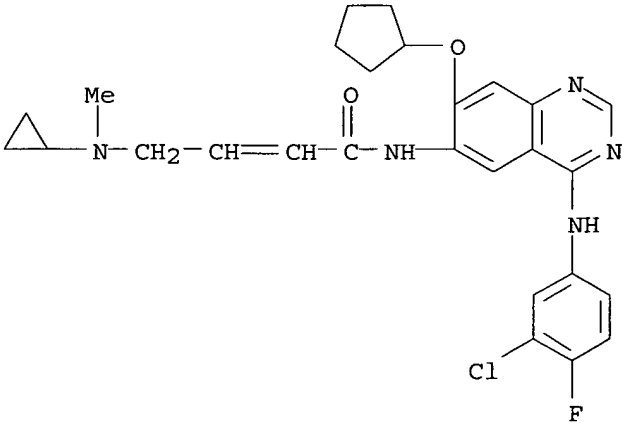
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-26-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



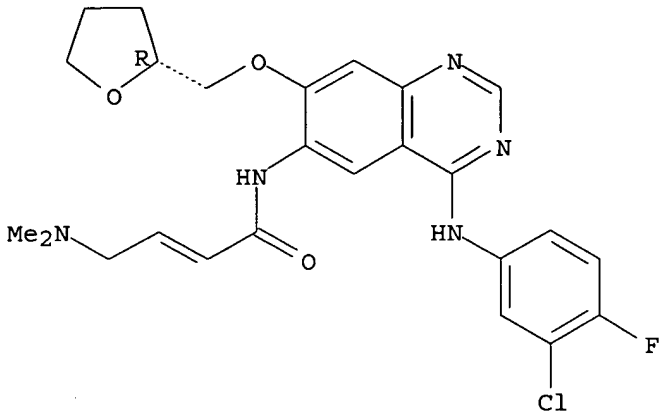
RN 439081-30-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)



RN 439081-39-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-

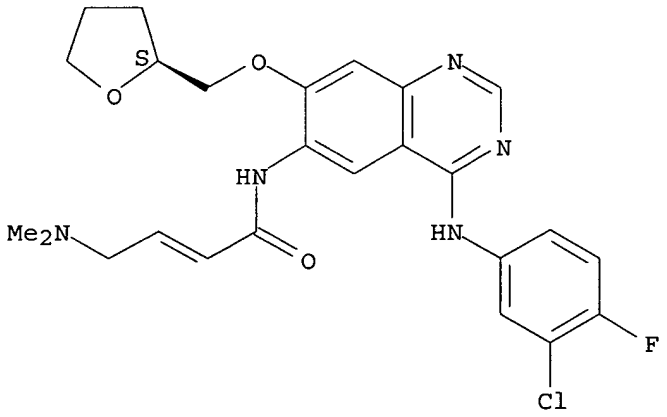
furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

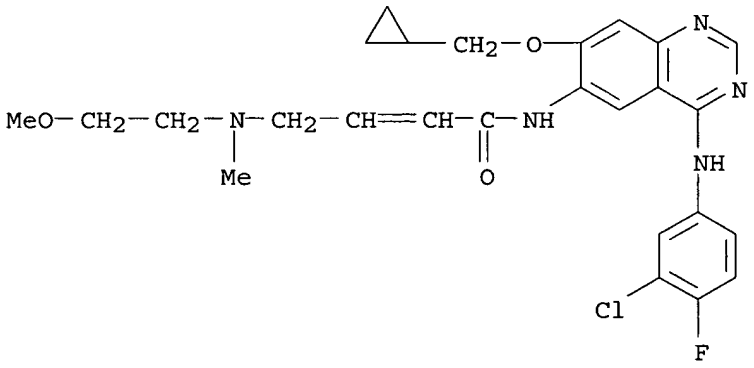


RN 439081-40-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

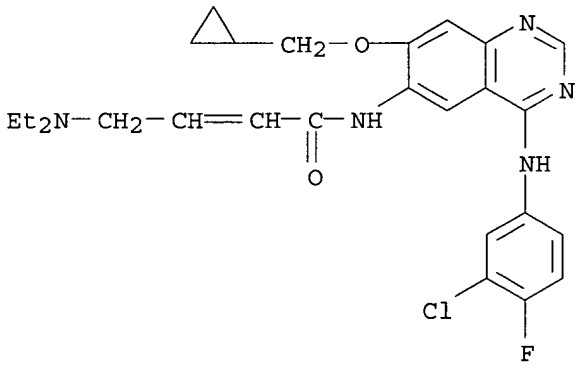
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-48-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



RN 573649-57-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



L8 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:570826 HCAPLUS
DOCUMENT NUMBER: 143:103193
TITLE: Optical imaging contrast agents for imaging lung cancer
INVENTOR(S): Klaveness, Jo; Johannesen, Edvin; Tolleshaug, Helge
PATENT ASSIGNEE(S): Amersham Health AS, Norway
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058370	A1	20050630	WO 2004-NO392	20041217

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: NO 2003-5681 A 20031218

AB The invention provides contrast agents for optical imaging of lung cancer in patients. The contrast agents may be used in diagnosis of lung cancer, for follow up of progress in disease development, for follow up of treatment of lung cancer and for surgical guidance. Further, the invention provides methods for optical imaging of lung cancer in patients.

IT **855309-69-2P**

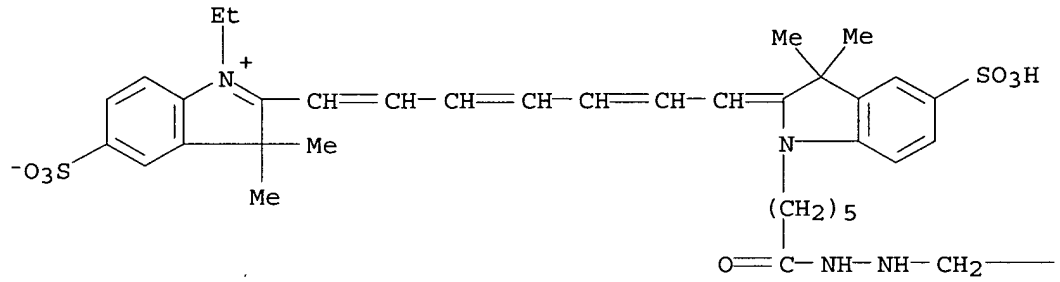
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(targeted imaging agents for lung cancer diagnosis)

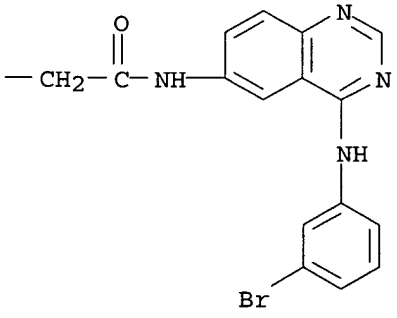
RN 855309-69-2 HCAPLUS

CN 3H-Indolium, 2-[7-[1-[6-[2-[3-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-3-oxopropyl]hydrazino]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene]-1,3,5-heptatrienyl]-1-ethyl-3,3-dimethyl-5-sulfo-, inner salt (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:567137 HCAPLUS
DOCUMENT NUMBER: 143:83434
TITLE: Optical imaging contrast agents for imaging of prostate cancer
INVENTOR(S): Klaveness, Jo; Johannesen, Edvin; Tolleshaug, Helge
PATENT ASSIGNEE(S): Amersham Health AS, Norway
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058372	A1	20050630	WO 2004-NO394	20041217

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

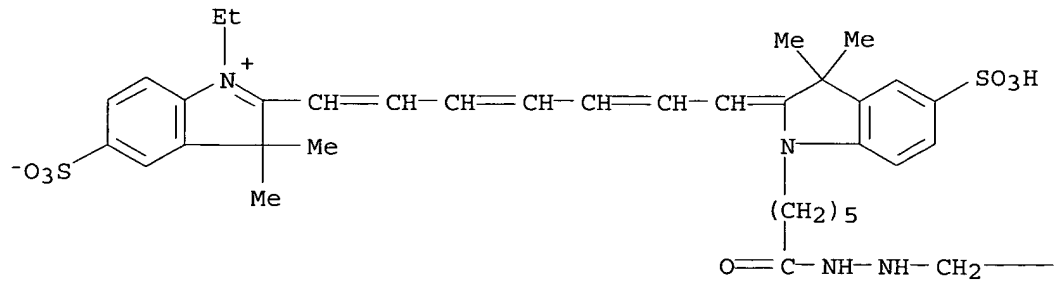
PRIORITY APPLN. INFO.: NO 2003-5683 A 20031218

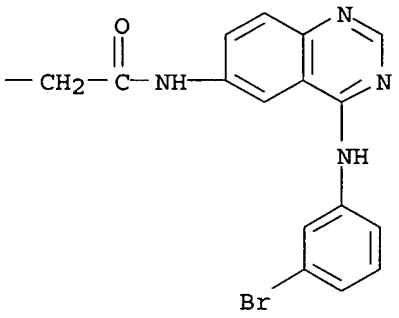
AB The invention provides contrast agents for optical imaging of prostate cancer in patients. The contrast agents may be used in diagnosis of prostate cancer, for follow up of progress in disease development, for follow up of treatment of prostate cancer and for surgical guidance. Further, the invention provides methods for optical imaging of prostate cancer in patients.

IT **855309-69-2P**
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(targeted contrast agents for imaging of prostate cancer)

RN 855309-69-2 HCAPLUS
CN 3H-Indolium, 2-[7-[1-[6-[2-[3-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-3-oxopropyl]hydrazino]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene]-1,3,5-heptatrienyl]-1-ethyl-3,3-dimethyl-5-sulfo-, inner salt (9CI) (CA INDEX NAME)

PAGE 1-A





REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:564588 HCAPLUS
DOCUMENT NUMBER: 143:103192
TITLE: Optical imaging contrast agents
INVENTOR(S): Klaveness, Jo; Johannesen, Edvin; Tolleshaug, Helge
PATENT ASSIGNEE(S): Amersham Health AS, Norway
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058371	A1	20050630	WO 2004-NO393	20041217

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: NO 2003-5682 A 20031218

AB The invention provides contrast agents for optical imaging of esophageal cancer and Barrett's esophagus in patients. The contrast agents may be used in diagnosis of esophageal cancer and Barrett's esophagus, for follow up of progress in disease development, for follow up of treatment of

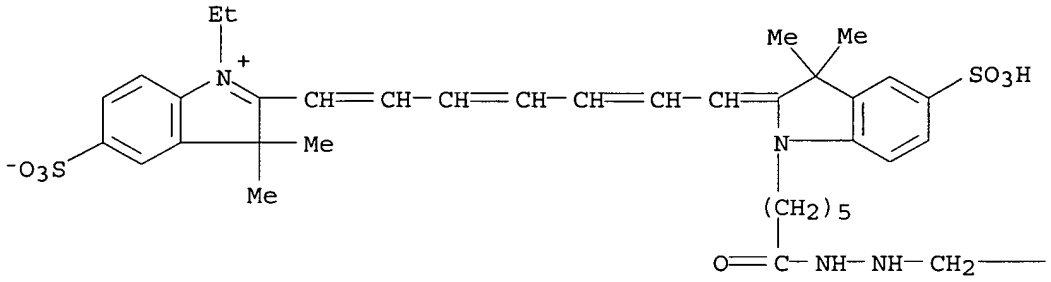
esophageal cancer and Barrett's esophagus and for surgical guidance. Further, the invention provides methods for optical imaging of esophageal cancer and Barrett's esophagus in patients.

IT **855309-69-2P**
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(optical imaging contrast agents targeted to esophageal cancer and Barrett's esophagus)

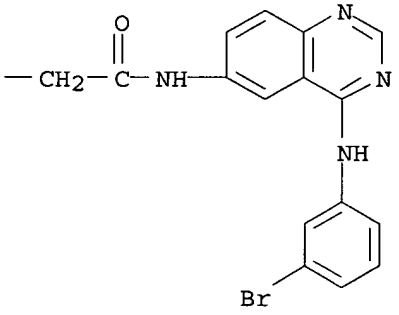
RN 855309-69-2 HCAPLUS

CN 3H-Indolium, 2-[7-[1-[6-[2-[3-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-3-oxopropyl]hydrazino]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene]-1,3,5-heptatrienyl]-1-ethyl-3,3-dimethyl-5-sulfo-, inner salt (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:349007 HCAPLUS
DOCUMENT NUMBER: 142:392435
TITLE: Synthesis of (oxobutenyl)quinazolines and derivatives for treating cancer and other diseases

INVENTOR(S): Soyka, Rainer; Rall, Werner; Schnaubelt, Juergen; Sieger, Peter; Kulinna, Christian
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005085495	A1	20050421	US 2004-941116	20040915
DE 10349113	A1	20050512	DE 2003-10349113	20031017
WO 2005037824	A2	20050428	WO 2004-EP11378	20041012
WO 2005037824	A3	20050721		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2003-10349113 A 20031017
US 2003-517777P P 20031106
OTHER SOURCE(S): MARPAT 142:392435
GI

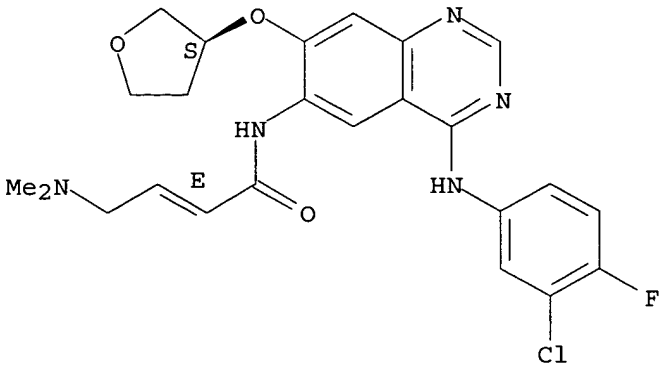
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to an improved process for preparing 4-[(3-chloro-4-fluorophenyl)amino]-6-{[4-(N,N-dimethylamino)-1-oxo-2-buten-1 -yl]amino}-7-[(S)-tetrahydrofuran-3-yloxy]quinazoline and related aminocrotonyl compds. I [Ra = CH2Ph, CH(Ph)Me, 3-Cl-4-FC6H3, R3, R4 = C1-C4-alkyl, X = C, N] and the preparation of a suitable salt of 4-[(3-chloro-4-fluorophenyl)amino]-6-{[4-(N,N-dimethylamino)-1 -oxo-2-buten-1 -yl]amino}-7-((S)-tetrahydrofuran-3-yloxy)-quinazoline for use as a pharmaceutically active substance. For example, reacting di-Et phosphonoacetic acid with quinazolinediamine II gave the corresponding phosphonate which was condensed with the aldehyde derived from (dimethylamino)acetaldehdye diethylacetal to give oxobutenyl compound III. Reaction of III with maleic acid gave the maleate salt.

IT **850140-72-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of (oxobutenyl)quinazolines and derivs. for treating cancer and diseases of the respiratory tract, lungs, gastrointestinal tract, bile duct, and gallbladder)

RN 850140-72-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

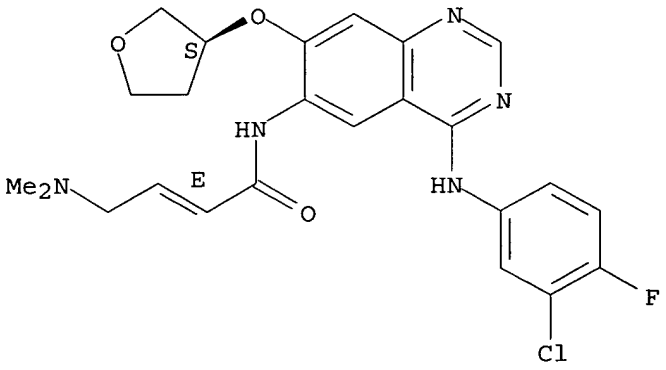


IT **850140-73-7P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of (oxobutenyl)quinazolines and derivs. for treating cancer and diseases of the respiratory tract, lungs, gastrointestinal tract, bile duct, and gallbladder and crystal structure)
RN 850140-73-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)-, (2E)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 850140-72-6
CMF C24 H25 Cl F N5 O3

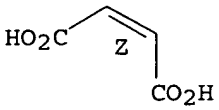
Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 110-16-7
CMF C4 H4 O4

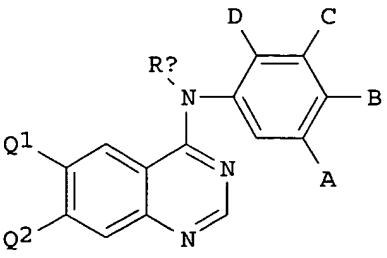
Double bond geometry as shown.



L8 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:238852 HCAPLUS
DOCUMENT NUMBER: 142:316852
TITLE: Preparation of radiolabeled 4-phenylaminoquinazoline derivatives as radiolabeled irreversible inhibitors of epidermal growth factor receptor tyrosine kinase and their use in radioimaging and radiotherapy
INVENTOR(S): Mishani, Eyal; Levitzki, Alexander; Ortu, Giuseppina; Ben-David, Iris; Rozen, Yulia
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; Hadasit Medical Research Services and Development Ltd.
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023315	A2	20050317	WO 2004-IL834	20040912
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004265228	A1	20041230	US 2003-659747	20030911
PRIORITY APPLN. INFO.:			US 2003-659747	A 20030911
			WO 2002-IL199	A2 20020312

OTHER SOURCE(S): MARPAT 142:316852
GI

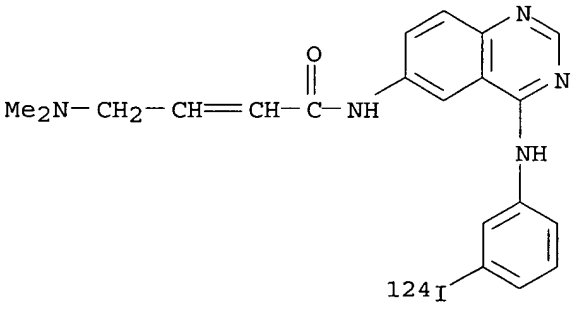


I

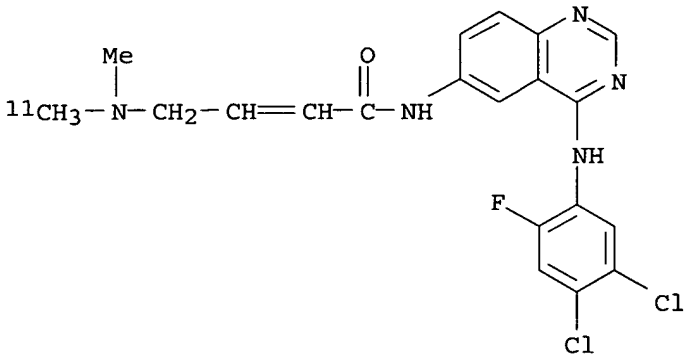
AB Radiolabeled 4-phenylaminoquinazoline derivs. (I) [wherein: Q1 = X-Y(:O)-Z and Q2 = H, halogen, alkoxy, HO, SH, thioalkoxy, alkylamino, or NH2; or Q1 = H, halogen, alkoxy, HO, SH, thioalkoxy, alkylamino, or NH2 and Q2 = X-Y(:O)-Z; X = -NR1-, -O-, -NH-NR1-, -O-NR1-, NH-CHR1-, -CHR1-NH-, -CHR1-O-, -O-CHR1-, -CHR1-CH2-, -CHR1-S-, or absent; Y = a nonradioactive or radioactive carbon; Z = R2C:CHR3, -C.tplbond.C-R3, -R2C:C:CHR3; Ra = H, C1-8 alkyl; A, B, C, D = H, a nonradioactive derivatizing group, a radioactive derivatizing group selected from a radioactive bromine, a radioactive iodine and a radioactive fluorine; R1 = H, (un)substituted C1-6 alkyl; R2 = H, halogen, C1-6 alkyl; R3 = each (un)substituted C1-6 alkyl or Ph; provided that the compound comprises at least one radioactive atom] are prepared These compds. are radiolabeled epidermal growth factor receptor tyrosine kinase (EGFR-TK) irreversible inhibitors and useful as biomarkers for medicinal radioimaging such as positron emission tomog. (PET) and single photon emission computed tomog. (SPECT) and as radiopharmaceuticals for radiotherapy are disclosed. Thus, carbon-11 labeled acryloyl chloride [11C:O] obtained from [11C]-CO2 (.apprx.700 mCi) and vinylmagnesium bromide, was reacted with 5-7 mg 4-[(3,4-dichloro-6-fluorophenyl)amino]-6-aminoquinazoline in 300 μL anhydrous THF for 2 min to give carbon 11-labeled N-[4-[(3,4-dichloro-6-fluorophenyl)amino]quinazolin-6-yl]acrylamide.

IT **746673-24-5P 848006-08-6P**
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of radiolabeled (phenylamino)quinazoline derivs. as radiolabeled irreversible inhibitors of epidermal growth factor receptor tyrosine kinase and their use in radioimaging and radiotherapy)

RN 746673-24-5 HCAPLUS
CN 2-Butenamide, 4-(dimethylamino)-N-[4-[[3-(iodo-124I)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

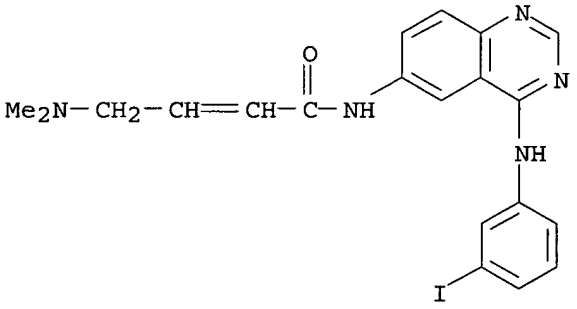


RN 848006-08-6 HCAPLUS
CN 2-Butenamide, N-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-quinazolinyl]-4-(methylmethyl-11C-amino)- (9CI) (CA INDEX NAME)

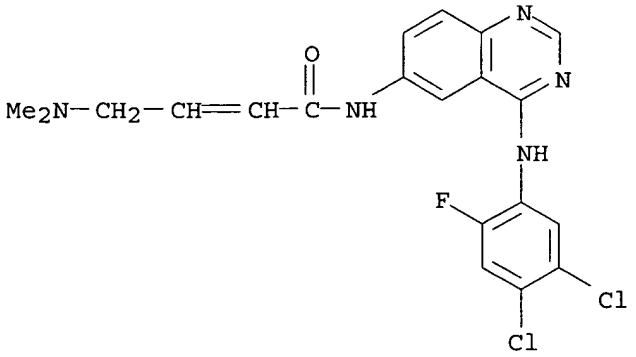


IT **746673-21-2P**, N-[4-[(3-Iodophenyl)amino]quinazolin-6-yl]-4-(dimethylamino)-2-butenamide **848006-05-3P**, N-[4-[(3,4-Dichloro-6-fluorophenyl)amino]quinazolin-6-yl]-4-(dimethylamino)-2-butenamide **848006-07-5P**, N-[4-[(3-Bromophenyl)amino]quinazolin-6-yl]-4-(methylamino)-2-butenamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of radiolabeled (phenylamino)quinazoline derivs. as radiolabeled irreversible inhibitors of epidermal growth factor receptor tyrosine kinase and their use in radioimaging and radiotherapy)

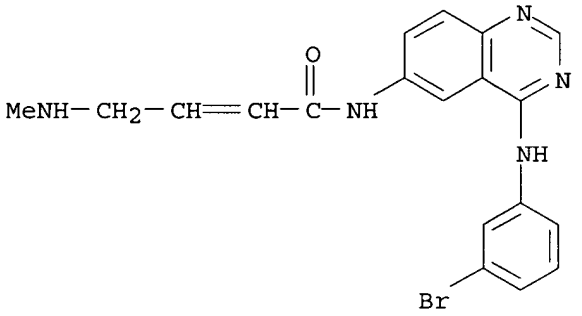
RN 746673-21-2 HCAPLUS
CN 2-Butenamide, 4-(dimethylamino)-N-[4-[(3-iodophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



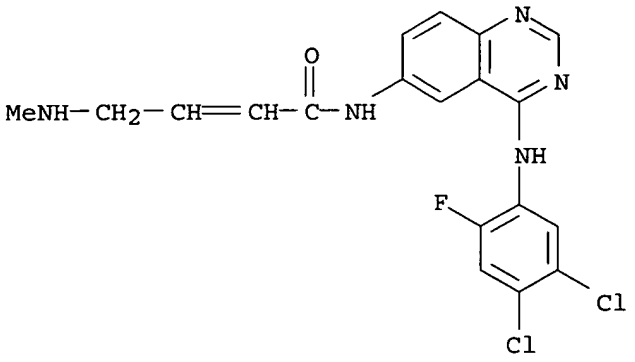
RN 848006-05-3 HCAPLUS
CN 2-Butenamide, N-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 848006-07-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(methylamino)-(9CI) (CA INDEX NAME)



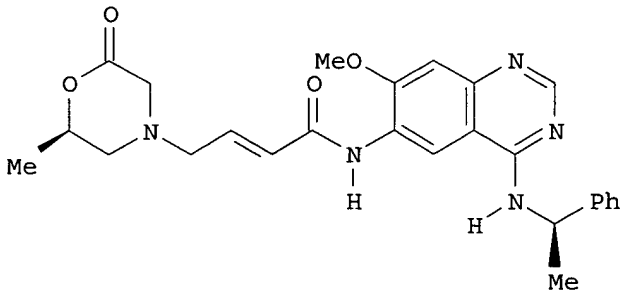
IT **848006-09-7P**, N-[4-[(3,4-Dichloro-6-fluorophenyl)amino]quinazolin-6-yl]-4-(methylamino)-2-butenamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of radiolabeled (phenylamino)quinazoline derivs. as radiolabeled irreversible inhibitors of epidermal growth factor receptor tyrosine kinase and their use in radioimaging and radiotherapy)
RN 848006-09-7 HCAPLUS
CN 2-Butenamide, N-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-quinazolinyl]-4-(methylamino)- (9CI) (CA INDEX NAME)



L8 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:120748 HCAPLUS
DOCUMENT NUMBER: 142:219295
TITLE: Preparation of quinazolines as tyrosine kinase inhibitors for the treatment of inflammatory illnesses
INVENTOR(S): Jung, Birgit; Pueschner, Hubert
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma GmbH & Co. KG
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005011701	A1	20050210	WO 2004-EP8185		20040722
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
DE 10334226	A1	20050217	DE 2003-10334226		20030728
US 2005059661	A1	20050317	US 2004-899817		20040727
PRIORITY APPLN. INFO.:			DE 2003-10334226	A	20030728
			US 2003-495540P	P	20030815

GI



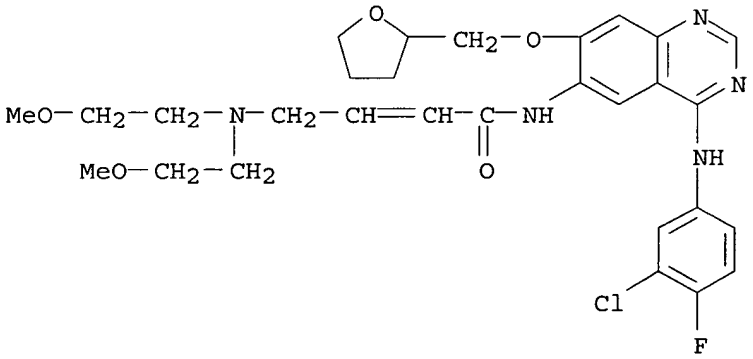
I

AB The title compds. and their pharmaceutically acceptable salts were claimed to be useful for the treatment of inflammatory illnesses. In cigarette smoke induced inflammatory assays, 5-examples of the title compds. exhibited ID50 [mg/kg] values ranging from 0.2-1.1, e.g., the ID50 value of quinazoline I was 0.3.

IT **439081-24-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines as tyrosine kinase inhibitors for the treatment of inflammatory illnesses)

RN 439081-24-0 HCAPLUS

CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:965067 HCAPLUS
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis
INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424
WO 2004096224	A3	20041216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1473043	A1	20041103	EP 2003-9587	20030429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
EP 2003-9587 A 20030429
EP 2004-508 A 20040113
EP 2004-1171 A 20040121

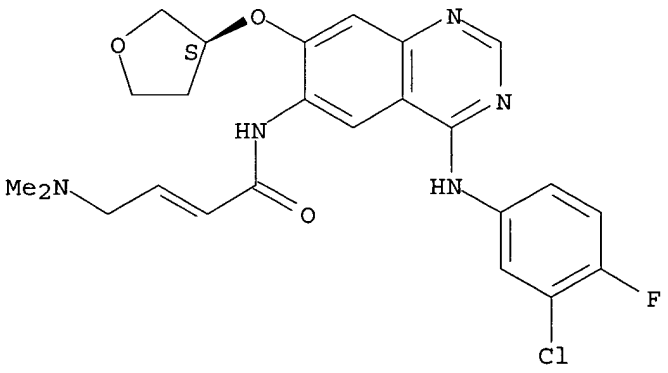
AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

IT **439081-18-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine kinase receptor antagonists and radiotherapy)

RN 439081-18-2 HCAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

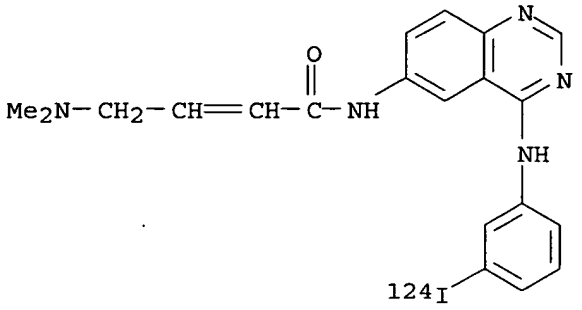
Absolute stereochemistry.
Double bond geometry unknown.



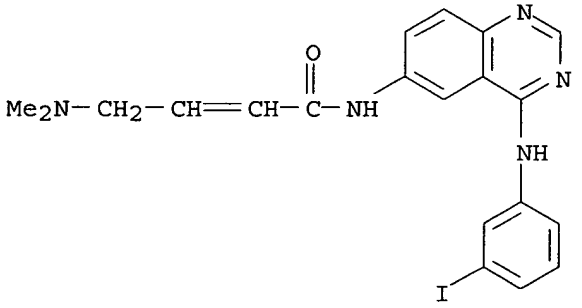
L8 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:469764 HCAPLUS
DOCUMENT NUMBER: 141:220981
TITLE: Novel iodine-124 labeled EGFR inhibitors as potential PET agents for molecular imaging in cancer
AUTHOR(S): Shaul, Mazal; Abourbeh, Galith; Jacobson, Orit; Rozen, Yulia; Laky, Desideriu; Levitzki, Alexander; Mishani, Eyal
CORPORATE SOURCE: Department of Medical Biophysics and Nuclear Medicine, Hadassah Hebrew University, Hadassah Hospital, Jerusalem, 91120, Israel
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(13), 3421-3429
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vivo results with our previously reported irreversible labeled inhibitor [11C]-ML03 suggested that more chemical stable inhibitors, labeled with a longer-lived radioisotope, could be better candidates for mol. imaging of epidermal growth factor receptor (EGFR) pos. tumors. On the basis of this hypothesis we synthesized three new irreversible tyrosine kinase (TK) inhibitors with various chemical reactivities. The three new inhibitors were successfully labeled on the anilino moiety with [124I], starting with the 6-amino-4-[(3-tributylstannylphenyl)amino]-quinazoline (9) precursor. The cell-free results, obtained with these new irreversible inhibitors, indicated that compds. 5 (α-chloro-acetamide derivative) and 6 (4-dimethylamino-but-2-enoic amide derivative) possessed high potencies toward the EGFR with an irreversible inhibition effect. Compound 4 (α-methoxy-acetamide derivative) was found to be less potent, with only a partially irreversible effect. The high potency of compds. 5 and 6 toward the EGFR establishes their potential as PET agents for mol. imaging of EGFR pos. tumors. Their prospect as PET biomarkers is further being investigated.

IT **746673-24-5P**
RL: DGN (Diagnostic use); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(124I-labeled EGFR inhibitors as potential PET agents for mol. imaging in cancer)
RN 746673-24-5 HCAPLUS
CN 2-Butenamide, 4-(dimethylamino)-N-[4-[[3-(iodo-124I)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



IT **746673-21-2P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(124I-labeled EGFR inhibitors as potential PET agents for mol. imaging in cancer)
RN 746673-21-2 HCAPLUS
CN 2-Butenamide, 4-(dimethylamino)-N-[4-[(3-iodophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

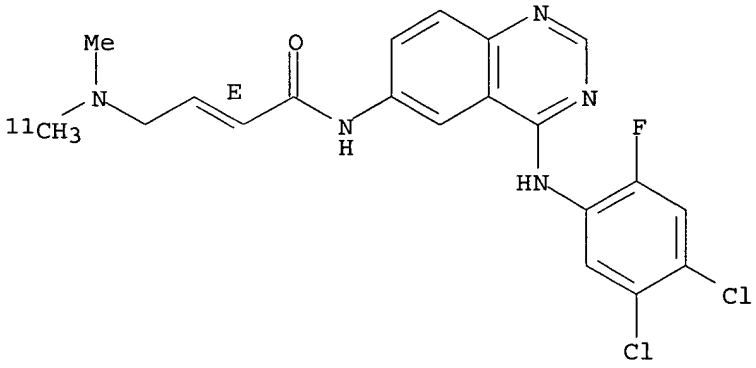
L8 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:320160 HCAPLUS
DOCUMENT NUMBER: 142:129832
TITLE: Novel carbon-11 labeled 4-dimethylamino-but-2-enoic acid [4-(phenylamino)-quinazoline-6-yl]-amides: potential PET bioprobes for molecular imaging of EGFR-positive tumors
AUTHOR(S): Mishani, Eyal; Abourbeh, Galith; Rozen, Yulia; Jacobson, Orit; Laky, Desideriu; Ben David, Iris; Levitzki, Alexander; Shaul, Mazal
CORPORATE SOURCE: Department of Nuclear Medicine, Hadassah Hebrew University Hospital, Jerusalem, 91120, Israel
SOURCE: Nuclear Medicine and Biology (2004), 31(4), 469-476
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have previously reported of labeled reversible and irreversible EGFR inhibitors, such as 4-(3,4-dichloro-6-fluoroanilino)-6,7-

dimethoxyquinazoline (ML01) and 6-acrylamido-4-(3,4-dichloro-6-fluoroanilino)quinazoline (ML03), to be suboptimal as imaging agents. On the basis of these studies, a new generation of novel, more chemical stable irreversible inhibitors was labeled with carbon-11 as potential positron emission tomog. (PET) biomarkers for mol. imaging of epidermal growth factor receptor (EGFR)-pos. tumors. In these new labeled, irreversible inhibitors the acryl-amide group at the 6-position of the quinazoline ring was replaced with a 4-dimethylamino-but-2-enoic amide. The nonlabeled compds. were evaluated in vitro to determine their EGFR autophosphorylation IC50 values. The IC50 values indicated that these new irreversible compds. possess similar potencies towards the EGFR, as the parent compound, ML03. These compds. were labeled with carbon-11 at the dimethylamine moiety, using the well known labeling reagent C-11 MeI. The labeling procedure was automated using a com. module. The final products were obtained with 10% decay corrected radiochem. yield, 99% radiochem. purity, 96% chemical purity, and a high specific activity of 2.7 Ci/μmol EOB. The high potency of these new labeled bioprobes towards the EGFR establishes their potential to serve as PET agents for mol. imaging of EGFR-pos. tumors.

IT **825615-00-7P 825615-01-8P 825615-03-0P**
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(11C-labeled dimethylamino-enoic acid phenylamino-quinazoline amides: potential PET agents for mol. imaging of EGFR-pos. tumors)

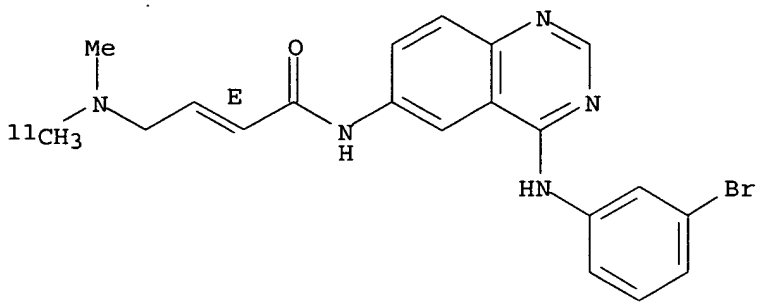
RN 825615-00-7 HCAPLUS
CN 2-Butenamide, N-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-quinazolinyl]-4-(methylmethyl-11C-amino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



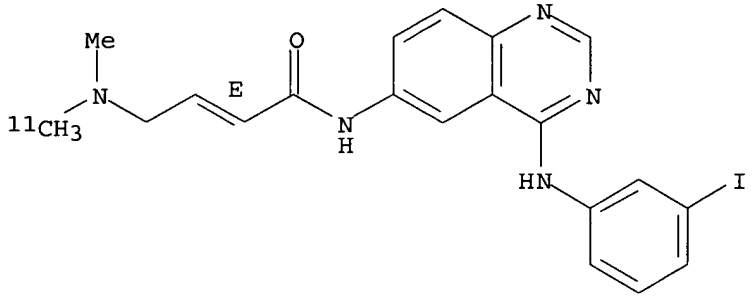
RN 825615-01-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(methylmethyl-11C-amino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



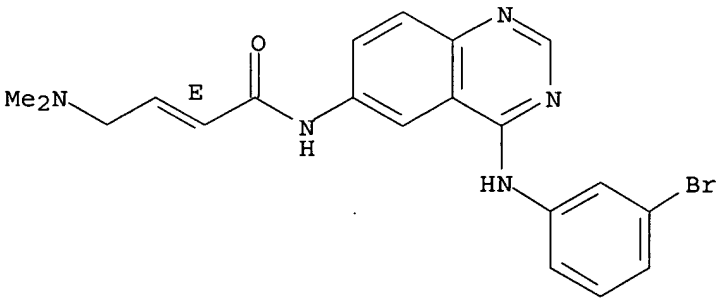
RN 825615-03-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-iodophenyl)amino]-6-quinazolinyl]-4-(methylmethyl-11C-amino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **361392-73-6P 825614-89-9P 825614-91-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(11C-labeled dimethylamino-enoic acid phenylamino-quinazoline amides: potential PET agents for mol. imaging of EGFR-pos. tumors)
RN 361392-73-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)-, (2E)- (9CI) (CA INDEX NAME)

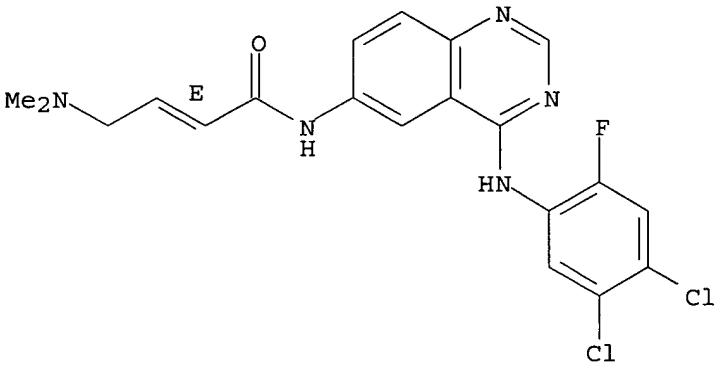
Double bond geometry as shown.



RN 825614-89-9 HCAPLUS
CN 2-Butenamide, N-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-quinazolinyl]-4-

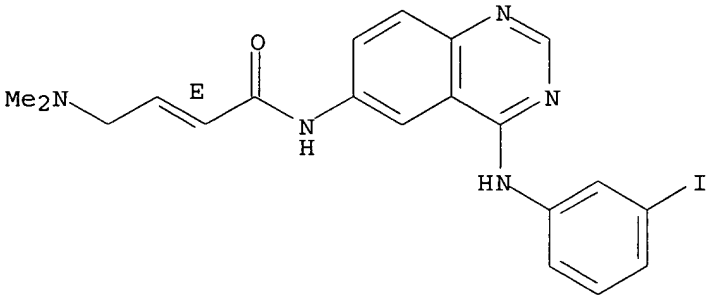
(dimethylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



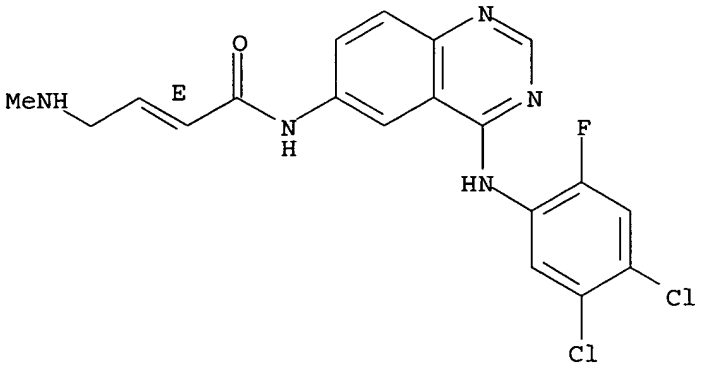
RN 825614-91-3 HCAPLUS
CN 2-Butenamide, 4-(dimethylamino)-N-[4-[(3-iodophenyl)amino]-6-quinazolinyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



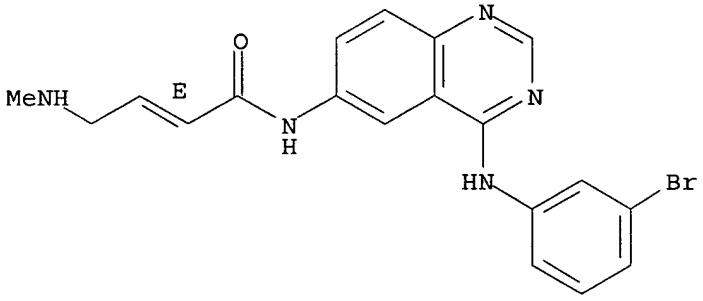
IT **825614-96-8P 825614-98-0P 825614-99-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(11C-labeled dimethylamino-enoic acid phenylamino-quinazoline amides: potential PET agents for mol. imaging of EGFR-pos. tumors)
RN 825614-96-8 HCAPLUS
CN 2-Butenamide, N-[4-[(4,5-dichloro-2-fluorophenyl)amino]-6-quinazolinyl]-4-(methylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



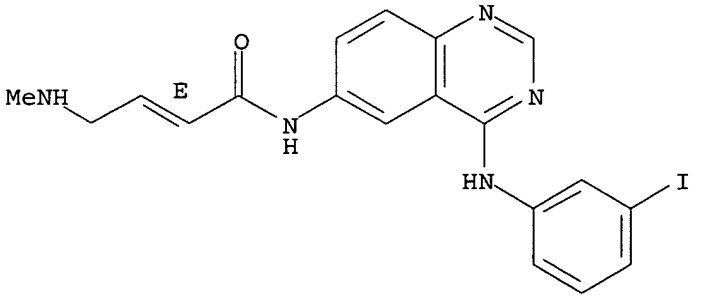
RN 825614-98-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(methylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 825614-99-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-iodophenyl)amino]-6-quinazolinyl]-4-(methylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41317 HCAPLUS
DOCUMENT NUMBER: 140:99649

TITLE: Pharmaceutical compositions for the treatment of respiratory tract diseases comprising novel anticholinergic agents and inhibitors of EGFR-kinase
INVENTOR(S): Pairet, Michel; Meade, Christopher John Montague; Pieper, Michael P.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004775	A1	20040115	WO 2003-EP6788	20030626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10230751	A1	20040122	DE 2002-10230751	20020709
CA 2492037	AA	20040115	CA 2003-2492037	20030626
BR 2003012507	A	20050412	BR 2003-12507	20030626
EP 1521595	A1	20050413	EP 2003-762525	20030626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004048887	A1	20040311	US 2003-614382	20030707
US 2005165013	A1	20050728	US 2005-87153	20050323

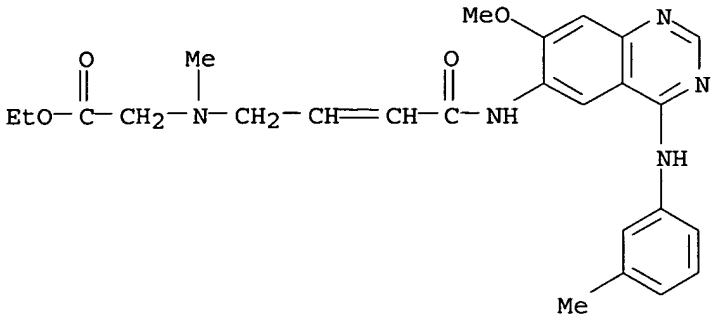
PRIORITY APPLN. INFO.:		
DE 2002-10230751	A	20020709
US 2002-407746P	P	20020903
WO 2003-EP6788	W	20030626
US 2003-614382	A1	20030707

OTHER SOURCE(S): MARPAT 140:99649

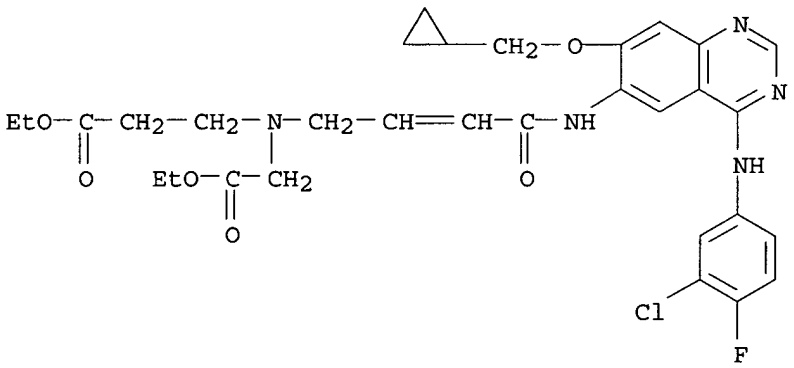
AB The invention relates to novel pharmaceutical compns. comprising novel anticholinergic agents and EGFR-kinase inhibitors, method for production and use thereof in the treatment of respiratory diseases. The synthesis of several EGFR-kinase inhibitors is given. Thus an inhalation capsule contained (microgram/capsule): 2,2-Diphenylpropionic acid scopine ester methobromide 60; EGFR kinase inhibitor 3500; lactose 3440.

IT **290301-86-9P 290302-19-1P 314771-10-3P**
439081-11-5P 439081-12-6P 439081-13-7P
439081-14-8P 439081-17-1P 439081-18-2P
439081-26-2P 439081-30-8P 439081-39-7P
439081-40-0P 439081-48-8P 573649-57-7P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. for treatment of respiratory tract diseases comprising anticholinergic agents and inhibitors of EGFR-kinase)

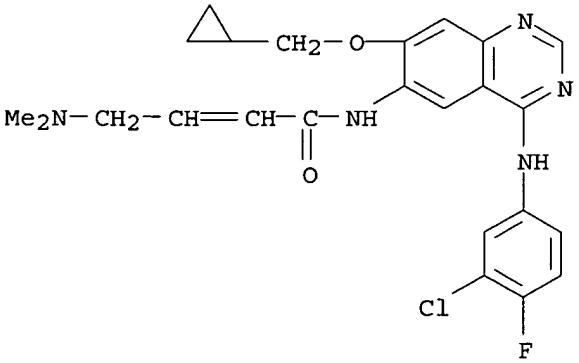
RN 290301-86-9 HCAPLUS
CN Glycine, N-[4-[[7-methoxy-4-[(3-methylphenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-19-1 HCAPLUS
CN β-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



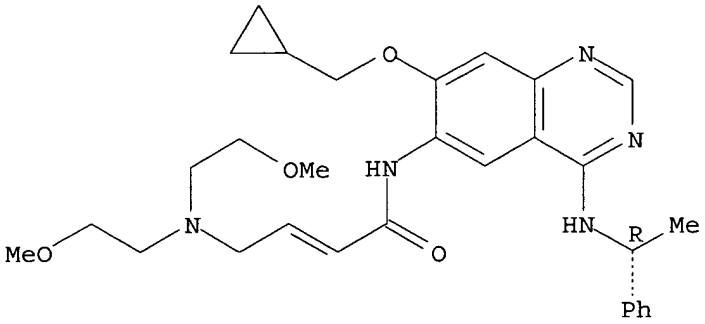
RN 314771-10-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 439081-11-5 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

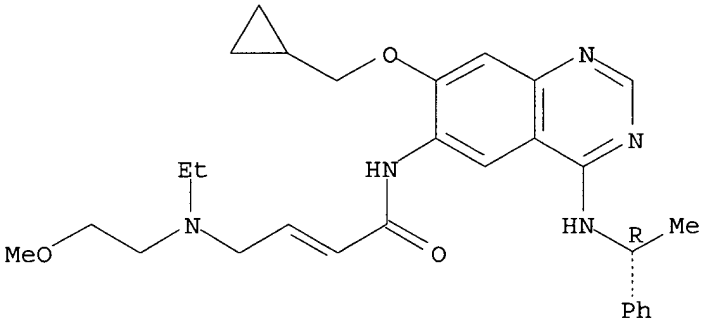
Absolute stereochemistry.

Double bond geometry unknown.



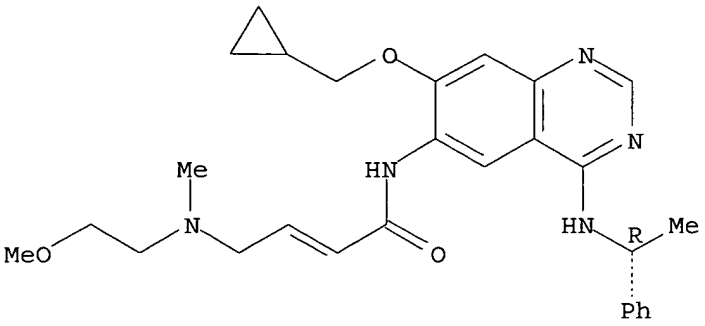
RN 439081-12-6 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-13-7 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

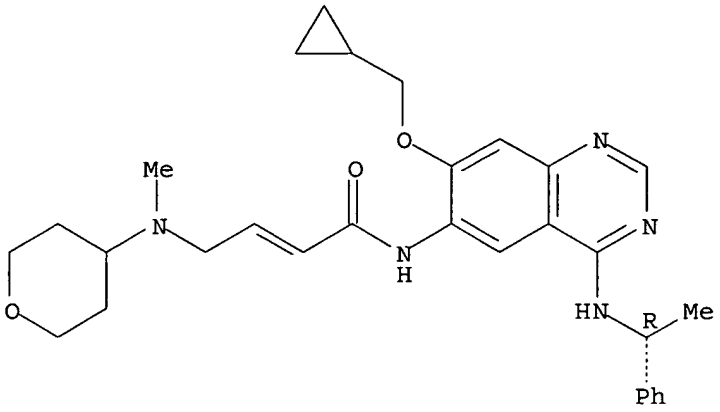
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-14-8 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-

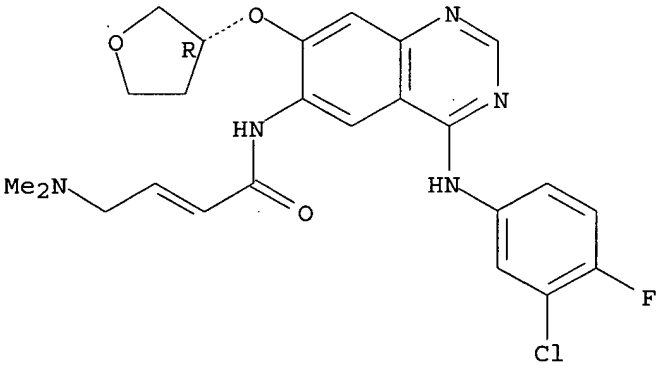
quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



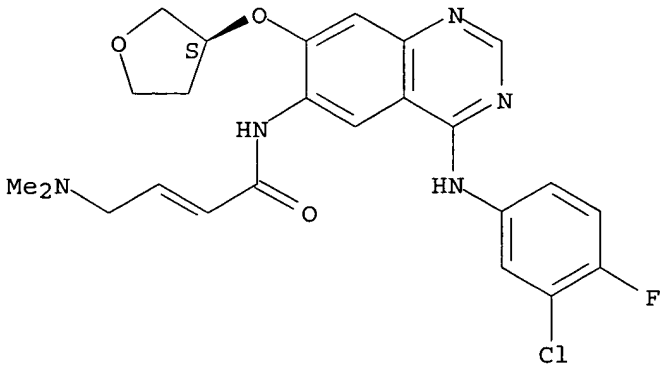
RN 439081-17-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

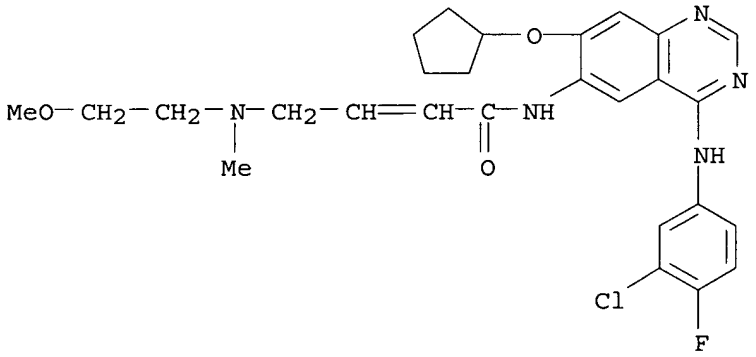


RN 439081-18-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

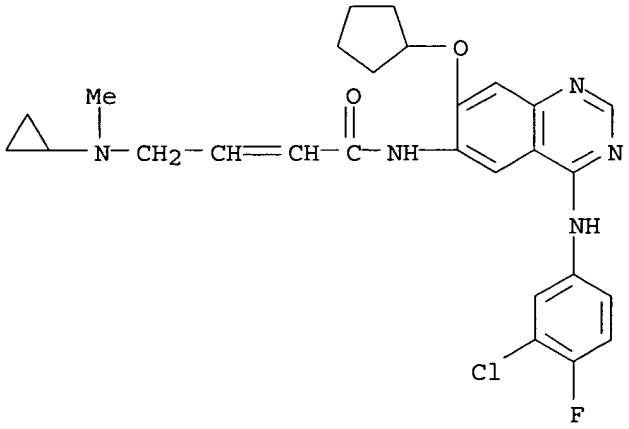
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-26-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



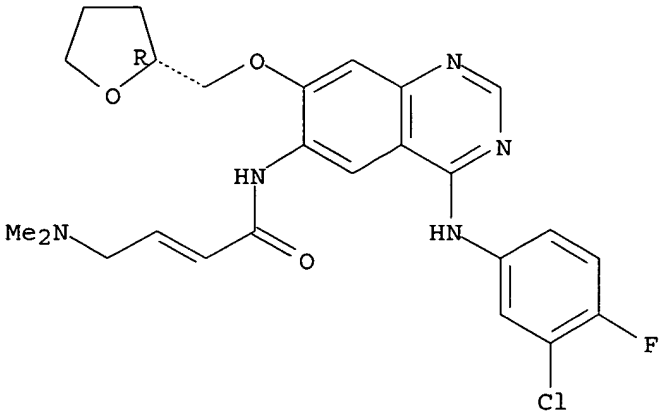
RN 439081-30-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)



RN 439081-39-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-

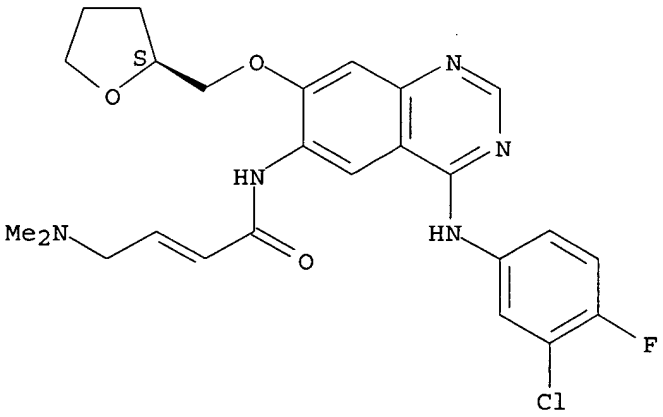
furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

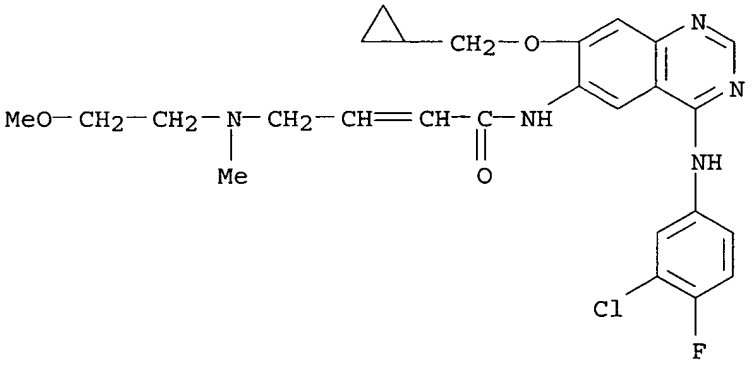


RN 439081-40-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

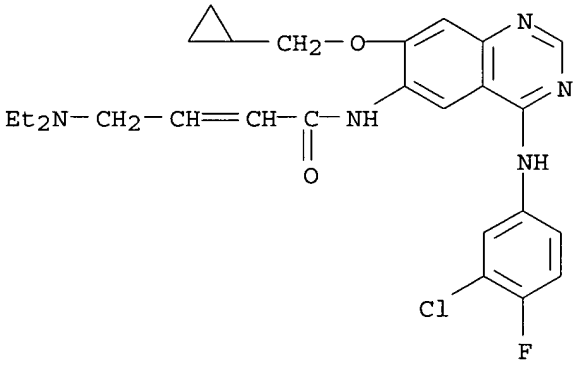
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-48-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

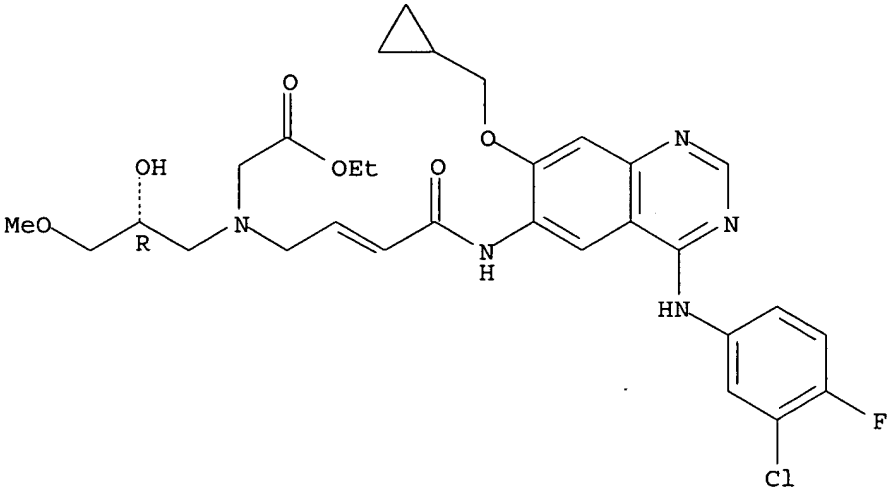


RN 573649-57-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



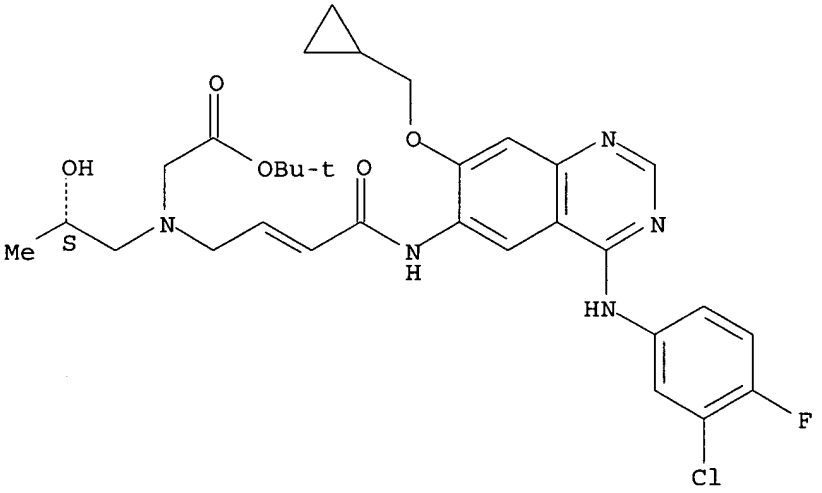
IT **402569-87-3 402855-15-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(pharmaceutical compns. for treatment of respiratory tract diseases comprising anticholinergic agents and inhibitors of EGFR-kinase)
RN 402569-87-3 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

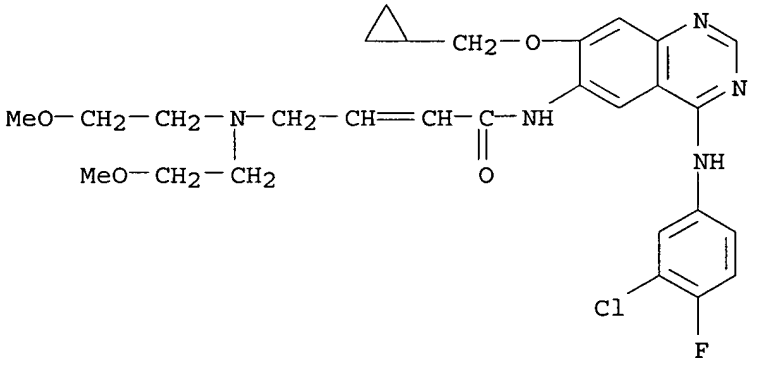


RN 402855-15-6 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



IT **314771-48-7**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for treatment of respiratory tract diseases comprising anticholinergic agents and inhibitors of EGFR-kinase)
RN 314771-48-7 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:913005 HCAPLUS
DOCUMENT NUMBER: 139:391384
TITLE: Use of inhibitors of EGFR-mediated signal transduction for the treatment of benign prostatic hyperplasia (BPH)/prostatic hypertrophy
INVENTOR(S): Singer, Thomas; Colbatzky, Florian; Platz, Stefan
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003094921	A2	20031120	WO 2003-EP4606	20030502
WO 2003094921	A3	20040318		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10221018	A1	20031127	DE 2002-10221018	20020511
CA 2483590	AA	20031120	CA 2003-2483590	20030502
EP 1505981	A2	20050216	EP 2003-727422	20030502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526123	T2	20050902	JP 2004-503006	20030502
US 2003225079	A1	20031204	US 2003-431699	20030508

PRIORITY APPLN. INFO.:

DE 2002-10221018	A	20020511
US 2002-389815P	P	20020618
WO 2003-EP4606	W	20030502

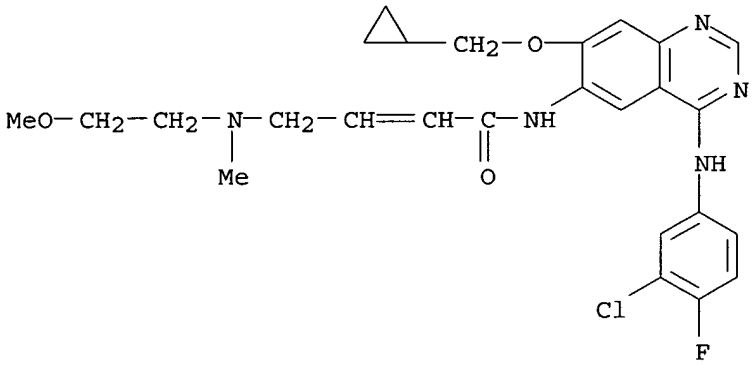
OTHER SOURCE(S): MARPAT 139:391384

AB The invention discloses the use of EGF-receptor antagonists for the production of a medicament to prevent and/or treat benign prostatic hyperplasia and/or prostatic hypertrophy, as well as a method for the treatment or prevention of benign prostatic hyperplasia/prostatic hypertrophy involving the administration of an EGF-receptor antagonist, optionally in combination with known compds. for the treatment of benign prostatic hyperplasia/prostatic hypertrophy, and the corresponding pharmaceutical compns. Compds. of the invention include e.g. quinazoline derivs. and monoclonal antibodies. Preparation of 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-(N-(2-methoxyethyl)-N-methylamino)-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline is described.

IT **439081-48-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(EGFR-mediated signal transduction inhibitors for treatment of benign prostatic hyperplasia/prostatic hypertrophy)

RN 439081-48-8 HCAPLUS

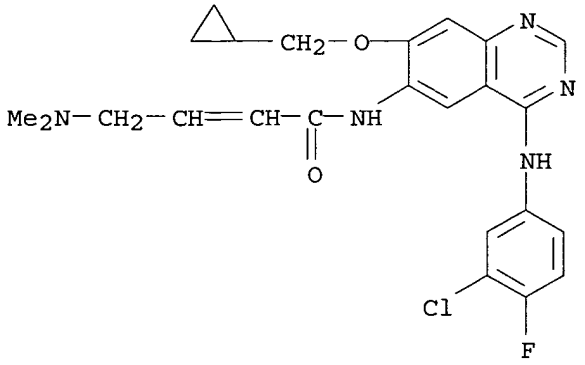
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



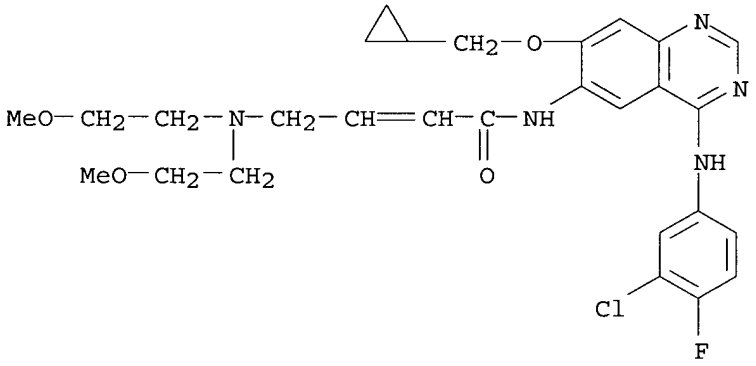
IT **314771-10-3 314771-48-7 439081-10-4 439081-17-1 439081-18-2 439081-26-2 439081-30-8 439081-39-7 439081-40-0 573649-57-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EGFR-mediated signal transduction inhibitors for treatment of benign prostatic hyperplasia/prostatic hypertrophy)

RN 314771-10-3 HCAPLUS

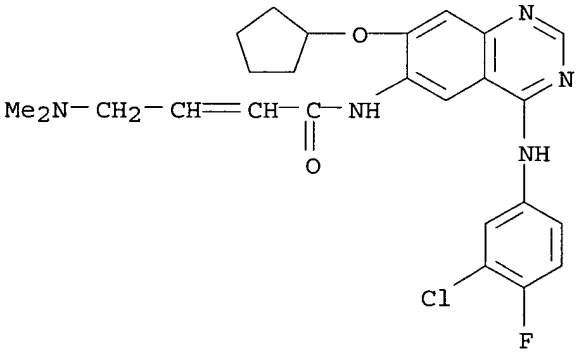
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 314771-48-7 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]- (9CI) (CA INDEX NAME)

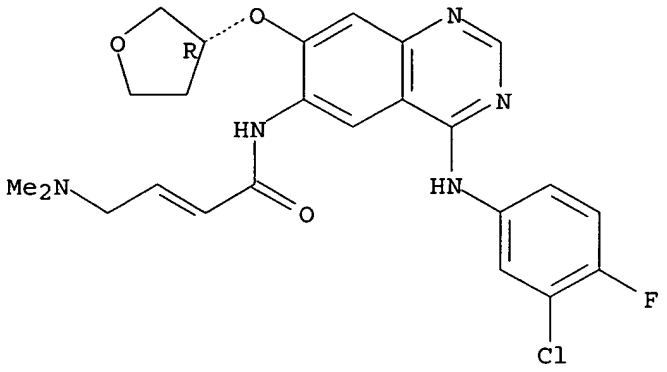


RN 439081-10-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



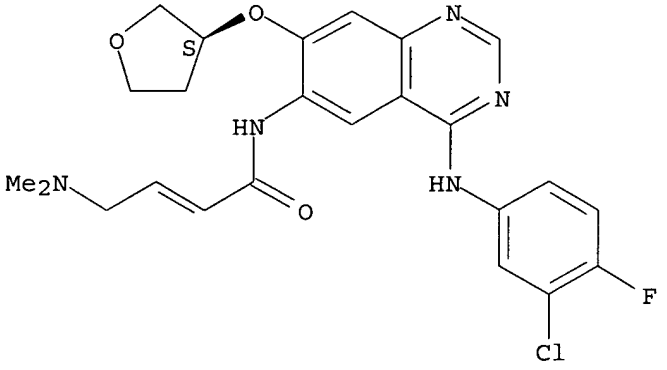
RN 439081-17-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

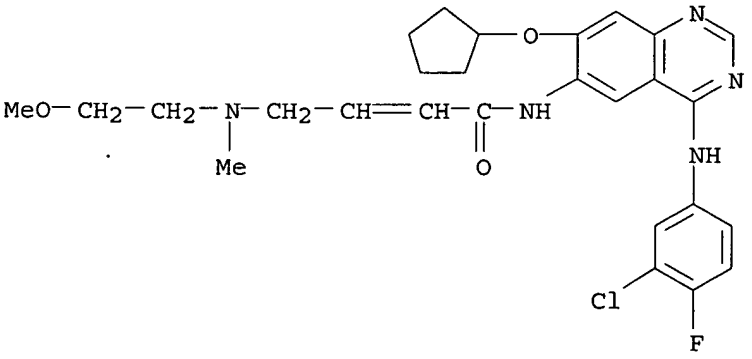


RN 439081-18-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

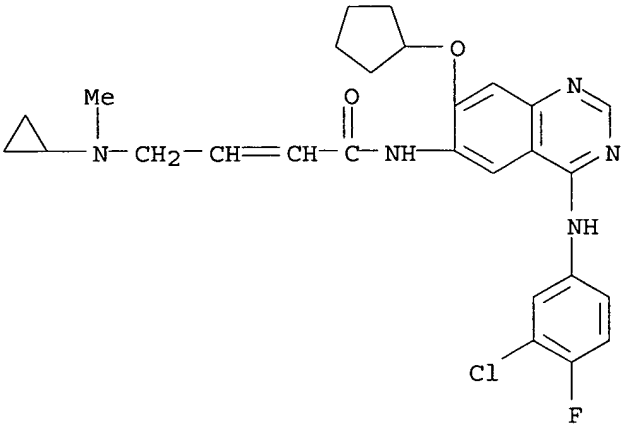
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-26-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

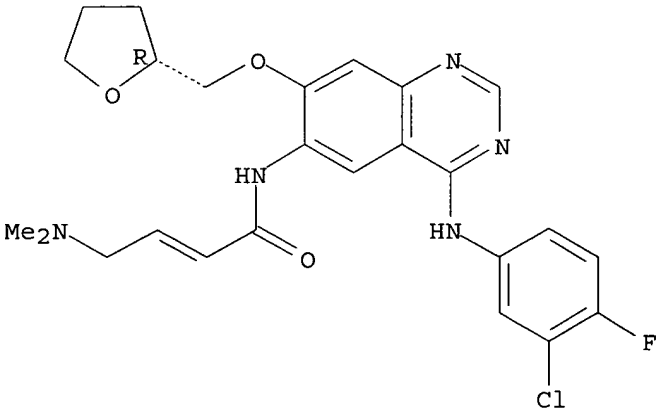


RN 439081-30-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)



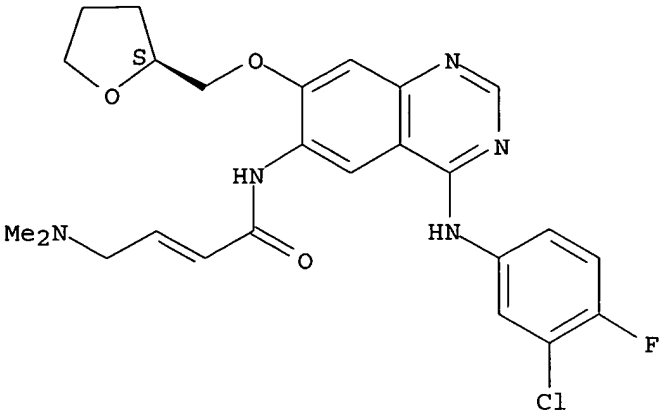
RN 439081-39-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

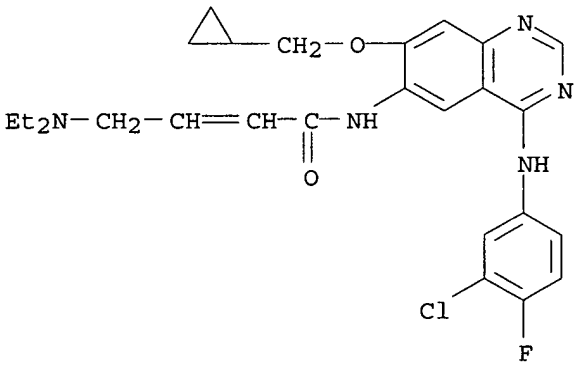


RN 439081-40-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 573649-57-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



L8 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:656610 HCAPLUS
DOCUMENT NUMBER: 139:202486
TITLE: Inhalants containing anticholinergic agents and EGFR kinase inhibitors
INVENTOR(S): Jung, Birgit; Pairet, Michel; Pieper, Michael P.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068264	A1	20030821	WO 2003-EP1357	20030212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

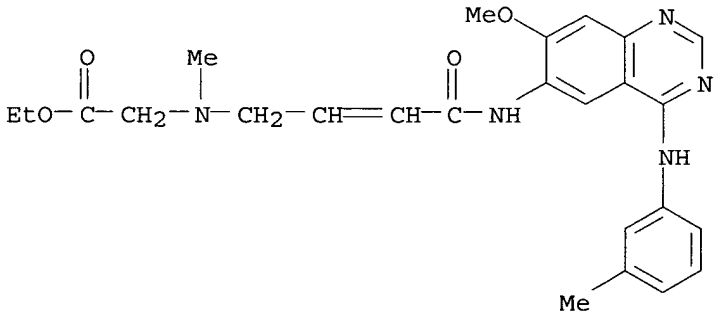
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10206505	A1	20030828	DE 2002-10206505		20020216
CA 2476127	AA	20030821	CA 2003-2476127		20030212
EP 1478398	A1	20041124	EP 2003-704593		20030212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003007703	A	20050104	BR 2003-7703		20030212
JP 2005517039	T2	20050609	JP 2003-567444		20030212
PRIORITY APPLN. INFO.:			DE 2002-10206505	A	20020216
			WO 2003-EP1357	W	20030212

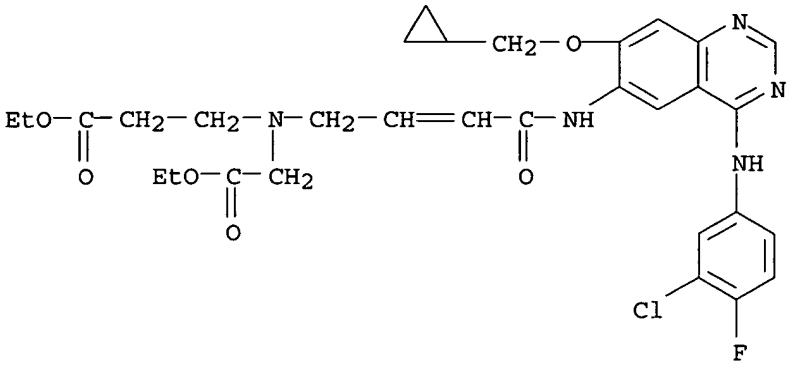
AB The invention relates to novel medicinal compns. on the basis of anticholinergic agents and EGFR kinase inhibitors, methods for their production and their use for treating respiratory diseases. Thus a series of quinazoline derivs. were synthesized that were EGFR kinase inhibitors. A typical inhalation powder contained (μg/capsule): tiotropium bromide 10.8; EGFR kinase inhibitor 3500; lactose 3489.2.

IT **290301-86-9P 290302-19-1P 314771-10-3P**
439081-10-4P 439081-11-5P 439081-12-6P
439081-13-7P 439081-14-8P 439081-17-1P
439081-18-2P 439081-26-2P 439081-30-8P
439081-48-8P 573649-57-7P 582311-86-2P
582311-87-3P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhalants containing anticholinergic agents and EGFR kinase inhibitors)

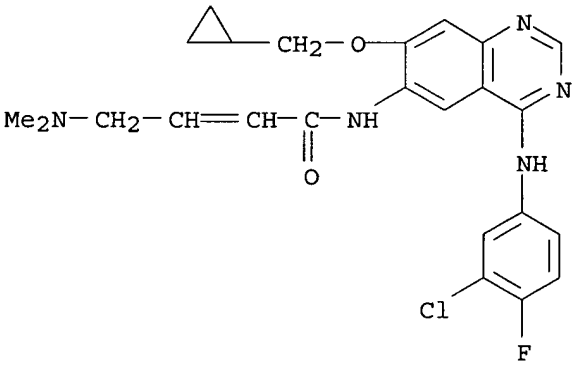
RN 290301-86-9 HCAPLUS
CN Glycine, N-[4-[[7-methoxy-4-[(3-methylphenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



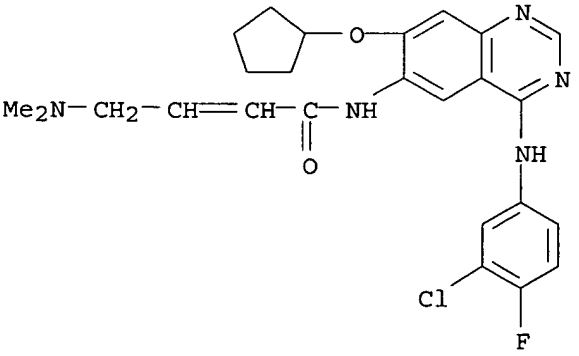
RN 290302-19-1 HCAPLUS
CN β-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 314771-10-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

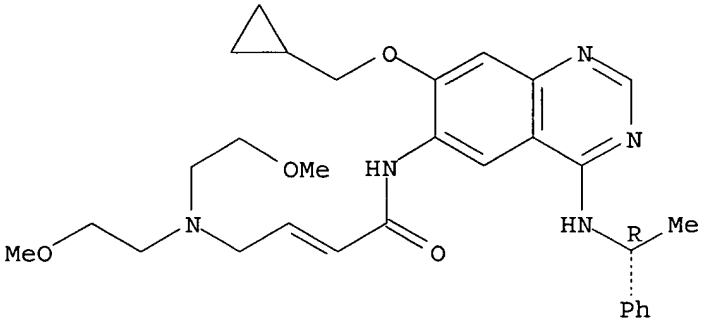


RN 439081-10-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



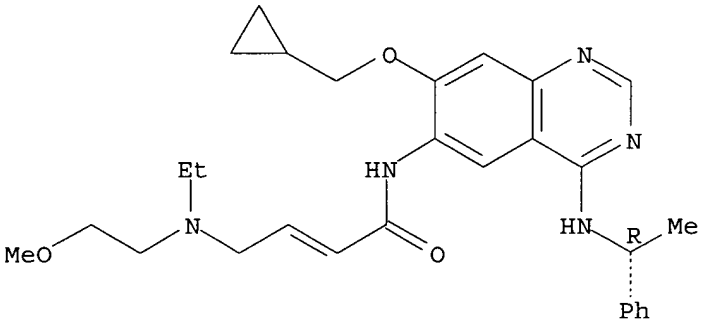
RN 439081-11-5 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



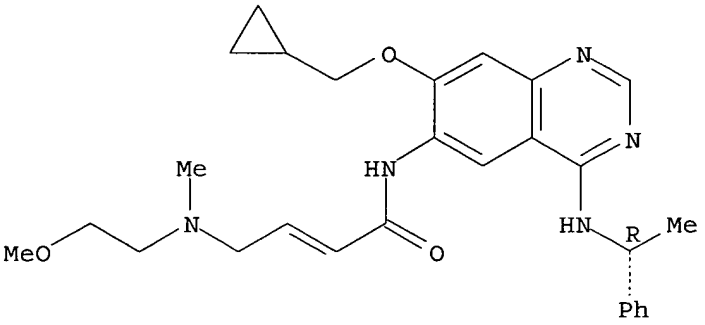
RN 439081-12-6 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-13-7 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

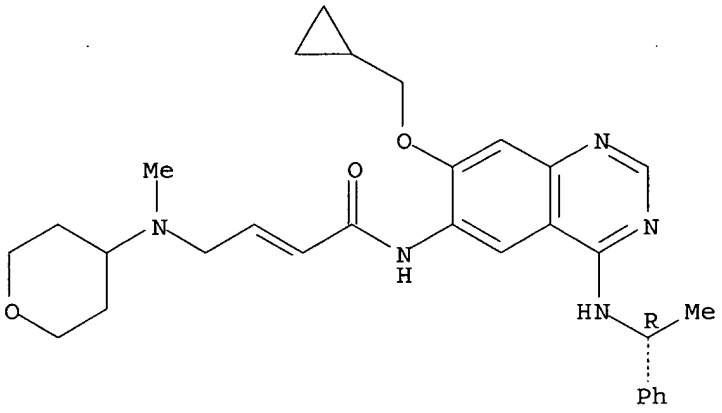
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-14-8 HCAPLUS

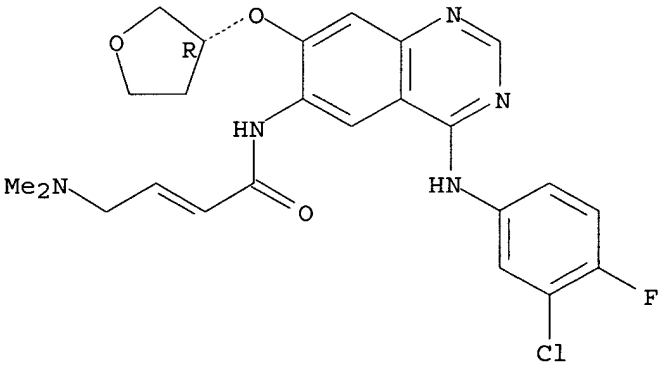
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



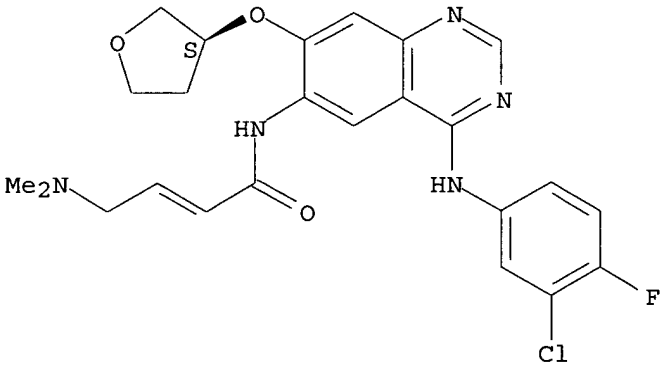
RN 439081-17-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

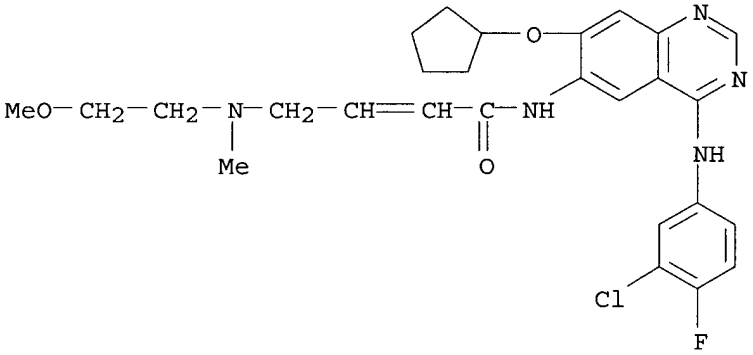


RN 439081-18-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

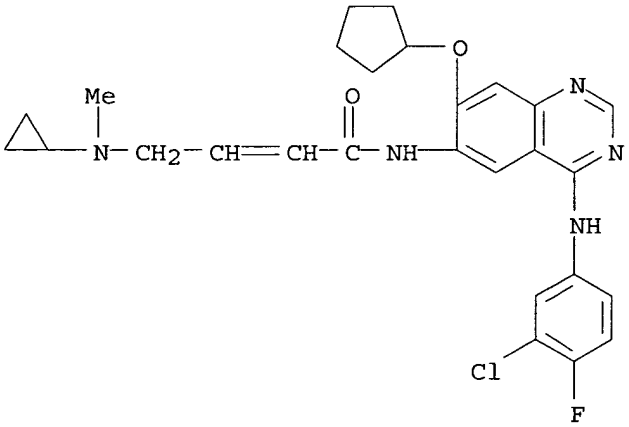
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-26-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

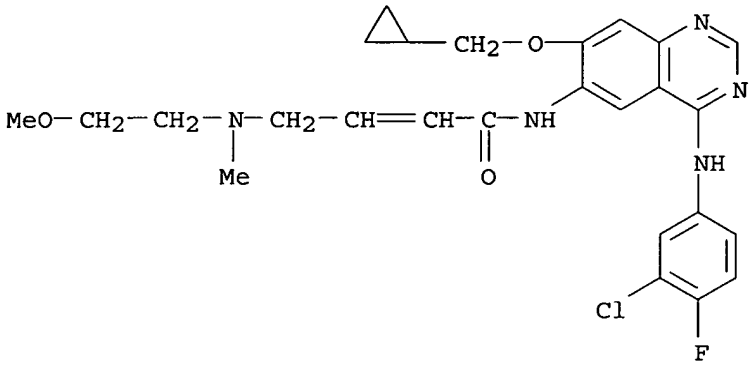


RN 439081-30-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)

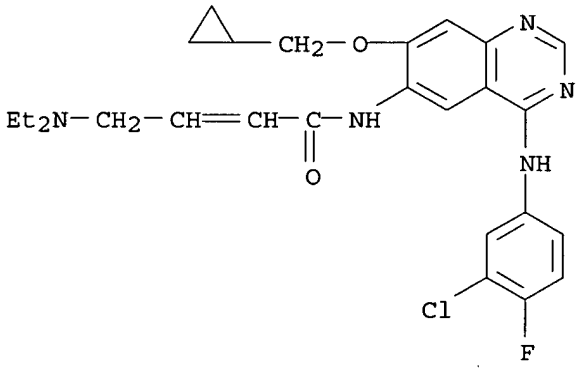


RN 439081-48-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-

6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

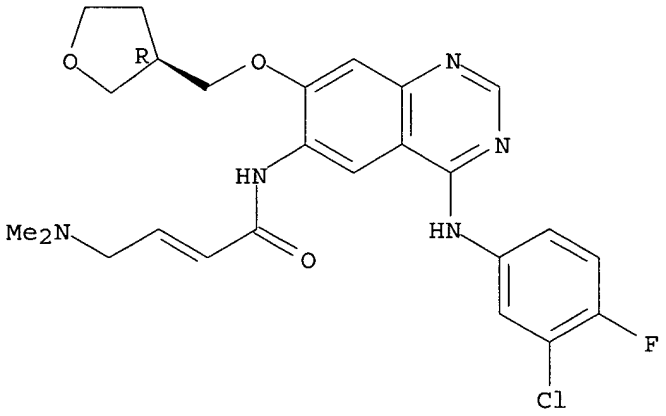


RN 573649-57-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



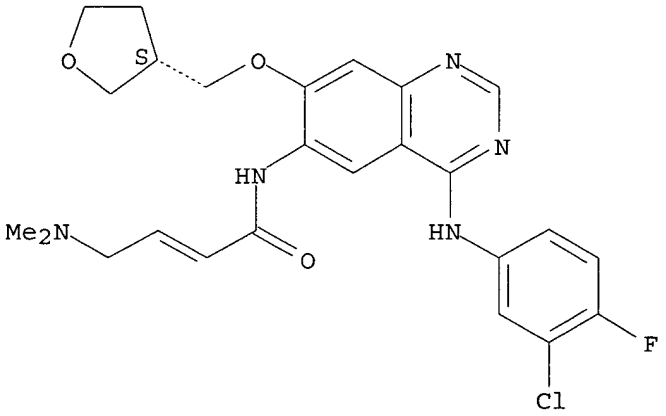
RN 582311-86-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



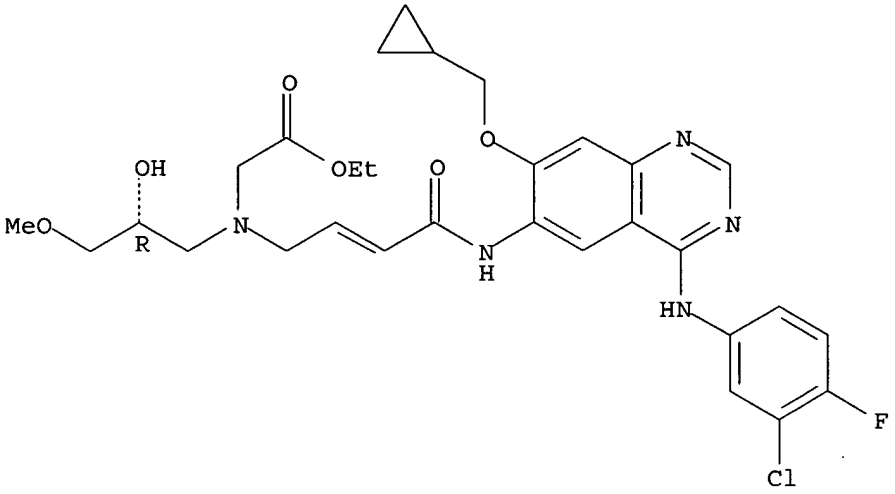
RN 582311-87-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



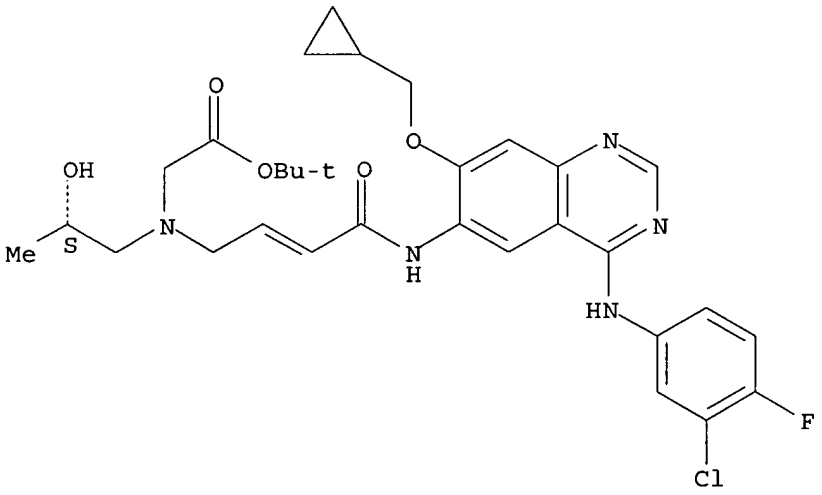
IT **402569-87-3 402855-15-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(inhalants containing anticholinergic agents and EGFR kinase inhibitors)
RN 402569-87-3 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

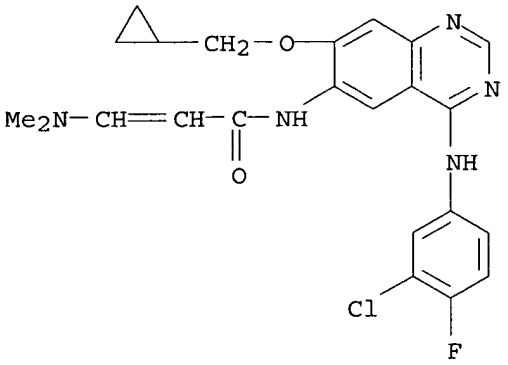


RN 402855-15-6 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



IT **582311-88-4**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalants containing anticholinergic agents and EGFR kinase inhibitors)
RN 582311-88-4 HCAPLUS
CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-3-(dimethylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:607455 HCAPLUS
DOCUMENT NUMBER: 139:159940
TITLE: Use of tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions
INVENTOR(S): Jung, Birgit; Puschner, Hubert
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10204462	A1	20030807	DE 2002-10204462	20020205
CA 2472293	AA	20030814	CA 2003-2472293	20030128
WO 2003066060	A2	20030814	WO 2003-EP814	20030128
WO 2003066060	A3	20040115		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1474149	A2	20041110	EP 2003-704477	20030128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005525328	T2	20050825	JP 2003-565484	20030128
US 2003149062	A1	20030807	US 2003-353616	20030129

PRIORITY APPLN. INFO.: DE 2002-10204462 A 20020205
WO 2003-EP814 W 20030128

OTHER SOURCE(S): MARPAT 139:159940

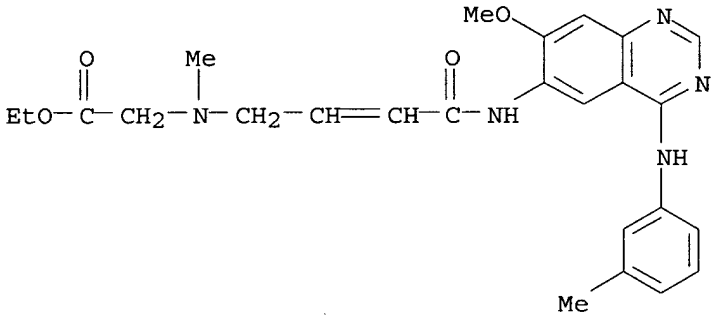
AB The invention discloses the use of quinazoline derivs. (Markush included), or the compds. (1) 4-[(3-chloro-4-fluorphenyl)amino]-6-[(4-

dimethylaminocyclohexyl)amino]pyrimido[5,4-d]pyrimidine; (2) 4-[(R)-(1-phenylethyl)amino]-6-(4-hydroxyphenyl)-7H-pyrrolo[2,3-d]pyrimidine; (3) 4-[(3-Chloro-4-(3-fluoro-4-benzyloxy)phenyl)amino]-6-[5-(((2-methansulfonylethyl)amino)methyl)-furan-2-yl]quinazoline; or the antibody cetuximab C225, trastuzumab, ABX-EGF, Mab ICR-62 and EGFR antisense, their tautomers, their stereoisomers and their salts, in particular their physiol. compatible salts with inorg. or organic acids or bases, for the production of a medication for prevention or treatment of diseases of the respiratory system or the lung. Preparation of quinazoline compds. is included.

IT **290301-86-9P 314771-48-7P 439081-10-4P**
439081-11-5P 439081-12-6P 439081-13-7P
439081-14-8P 439081-17-1P 439081-18-2P
439081-26-2P 439081-30-8P 439081-39-7P
439081-40-0P 439081-48-8P 573649-57-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)

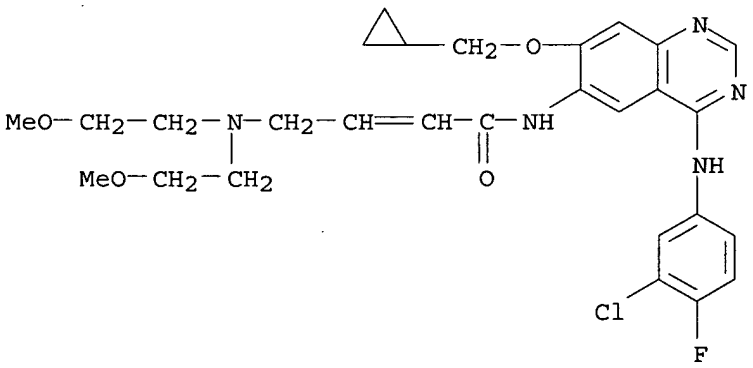
RN 290301-86-9 HCAPLUS

CN Glycine, N-[4-[[7-methoxy-4-[(3-methylphenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



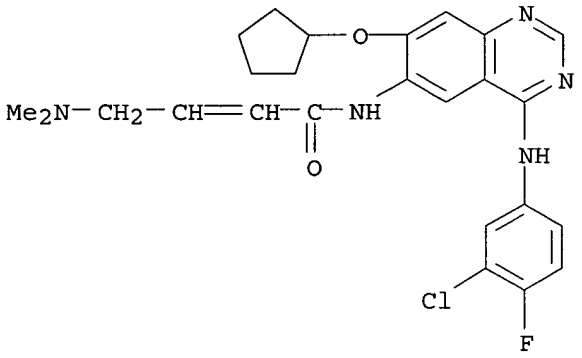
RN 314771-48-7 HCAPLUS

CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



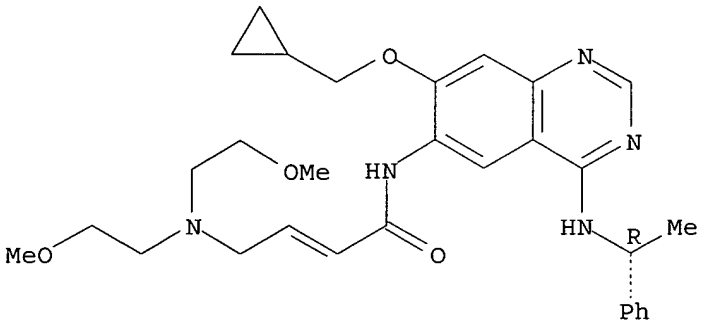
RN 439081-10-4 HCAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



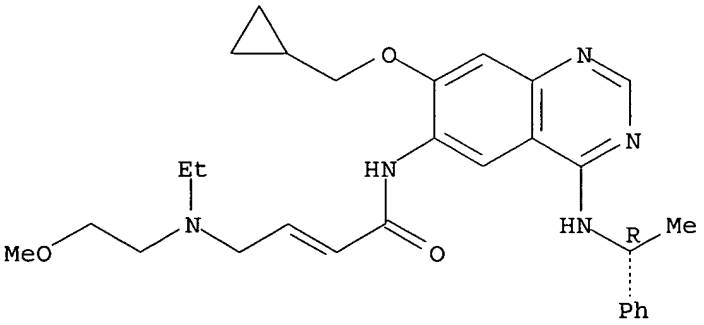
RN 439081-11-5 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



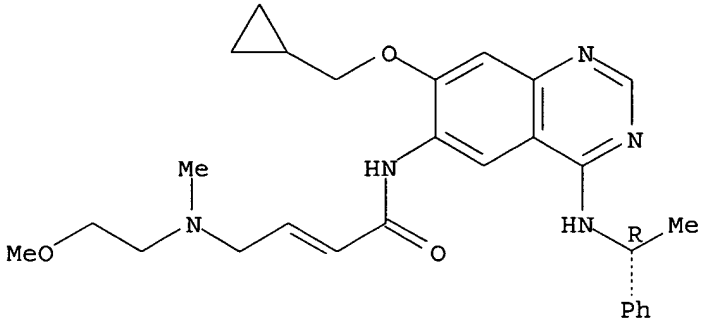
RN 439081-12-6 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



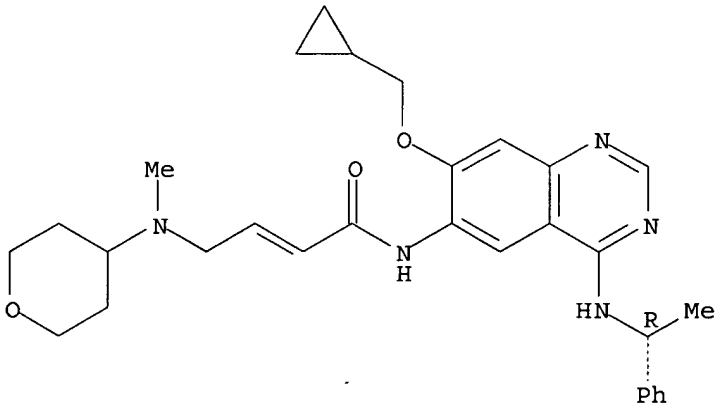
RN 439081-13-7 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



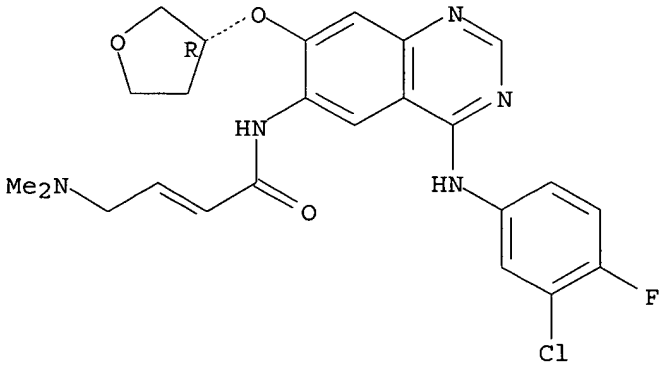
RN 439081-14-8 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



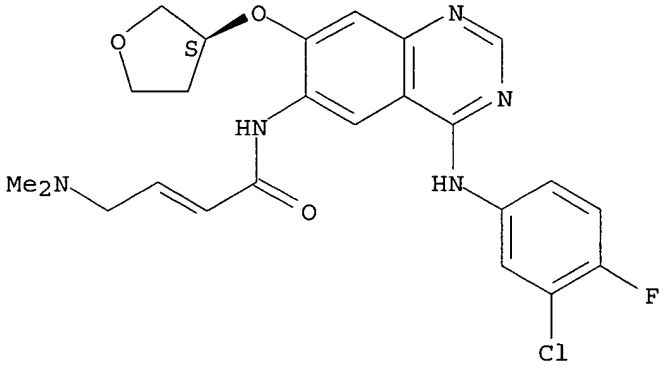
RN 439081-17-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

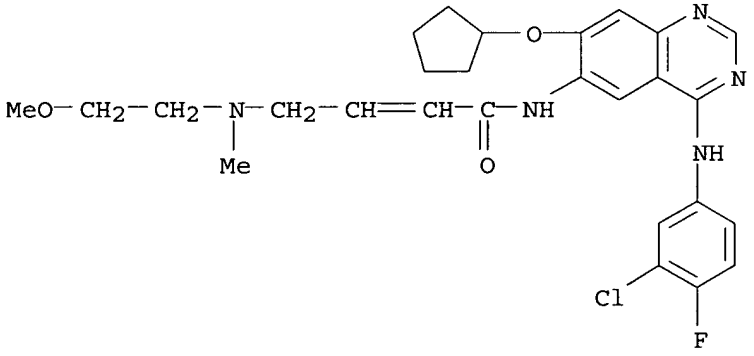


RN 439081-18-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

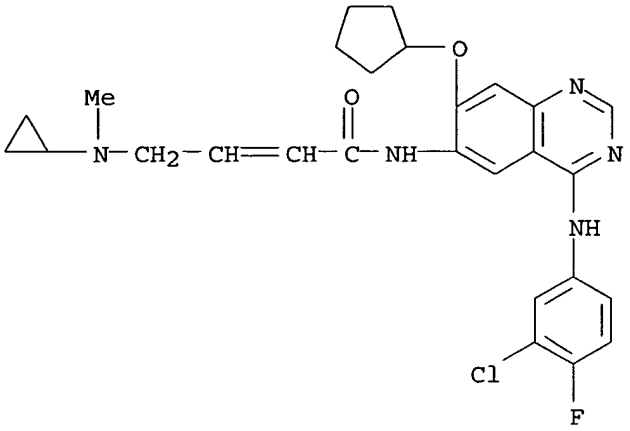


RN 439081-26-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



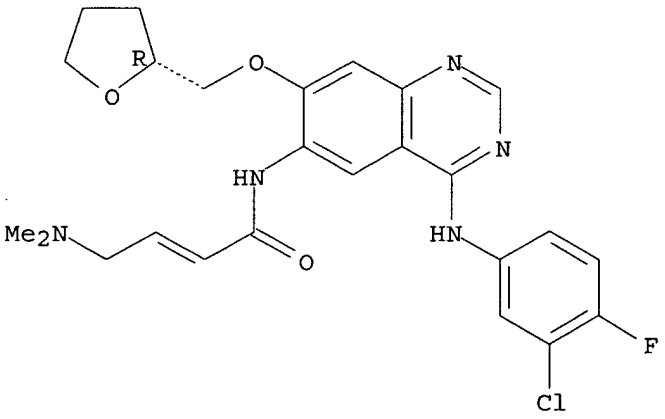
RN 439081-30-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-

quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)



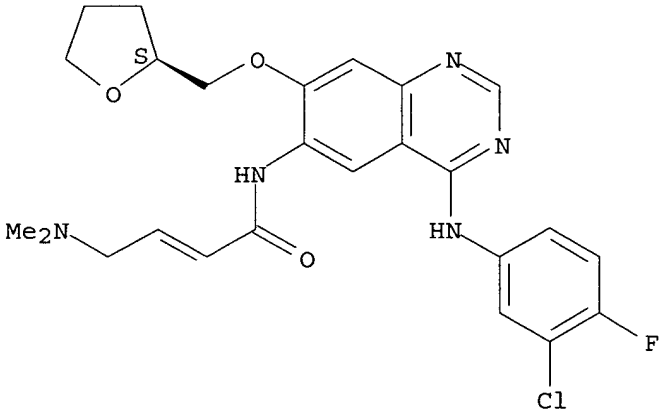
RN 439081-39-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

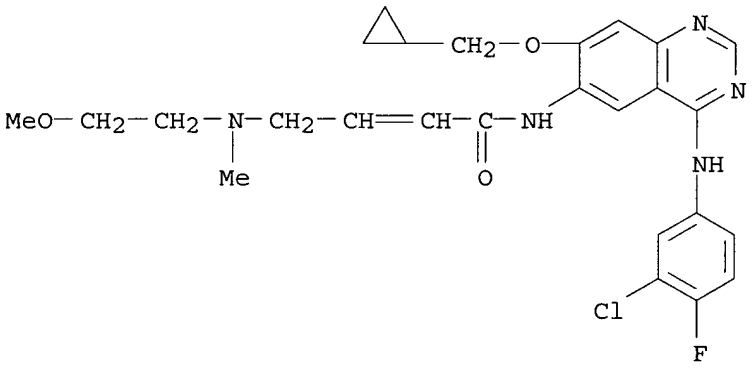


RN 439081-40-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

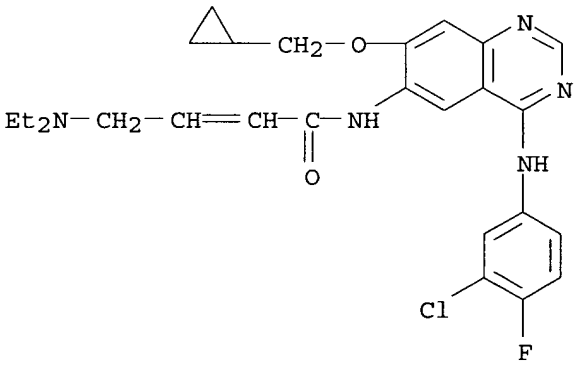
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-48-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



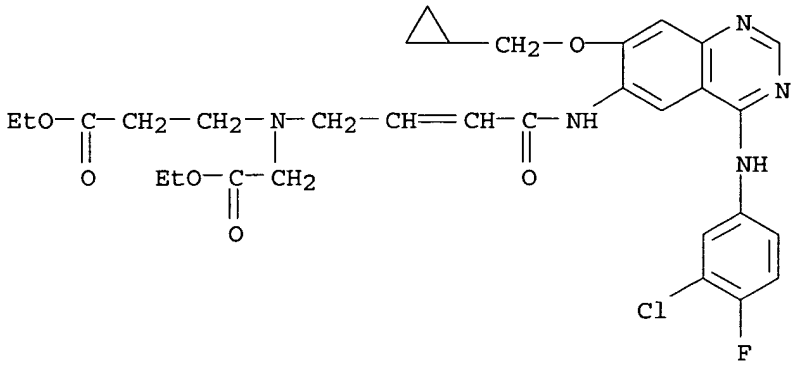
RN 573649-57-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



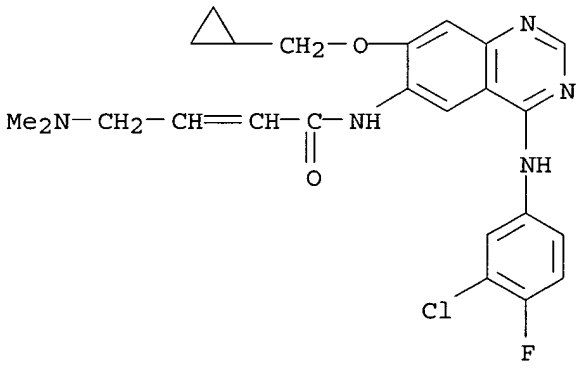
IT **290302-19-1 314771-10-3 573649-60-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)

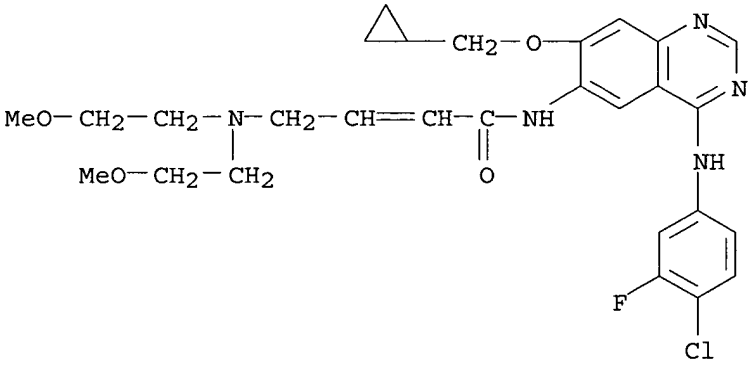
RN 290302-19-1 HCAPLUS
CN β-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 314771-10-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

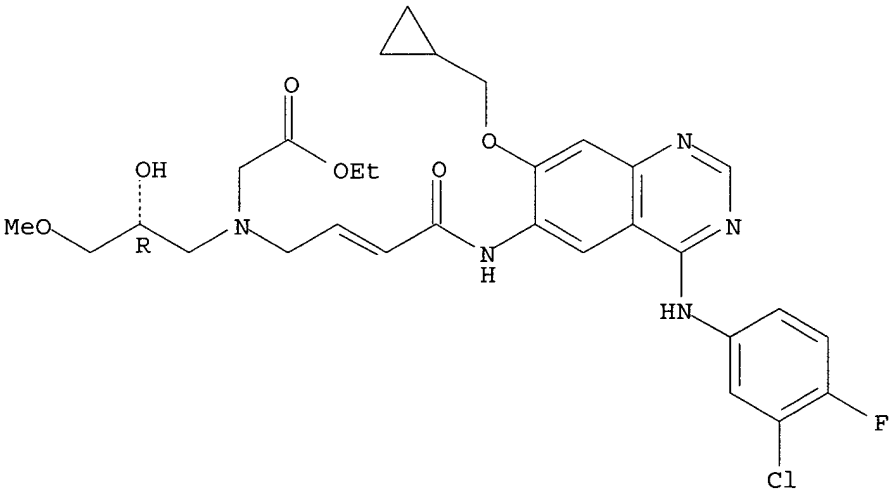


RN 573649-60-2 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(4-chloro-3-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



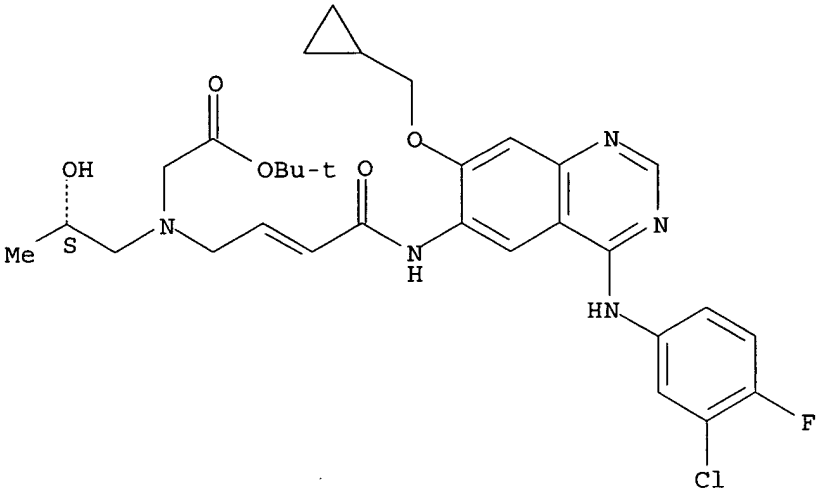
IT **402569-87-3 402855-15-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(tyrosine kinase inhibitors for treatment of pulmonary inflammatory conditions)
RN 402569-87-3 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-15-6 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

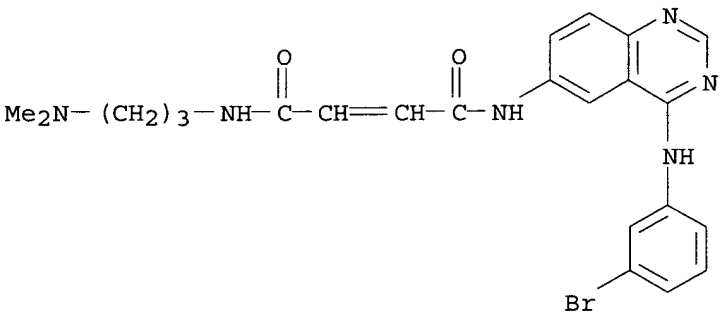
Absolute stereochemistry.
Double bond geometry unknown.



L8 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:52764 HCAPLUS
DOCUMENT NUMBER: 139:390698
TITLE: Searching for allosteric effects via QSAR. Part II
AUTHOR(S): Garg, Rajni; Kurup, Alka; Mekapati, Suresh B.; Hansch, Corwin
CORPORATE SOURCE: Department of Chemistry, Pomona College, Claremont, CA, 91711, USA
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(4), 621-628
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Allosteric interactions have in the past been established by x-ray crystallog. or careful study of a single mol. at a variety of concns. Here the authors report a method for using QSAR to establish a change in reaction mechanism by establishing an inversion point. That is, as polarizability of a member of a congeneric set of compds. is increased (as measured by calculated mol. refractivity (CMR)), activity at first decreases until, at the inversion, activity turns around and increases. Out of 23 examples, 14 have inversion points of 10. This includes a wide variety of receptors such as thrombin, 5-HT, dopamine, and tyrosine kinase acting with a variety of ligands.

IT **198961-42-1**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(epidermal growth factor receptor tyrosine kinase autophosphorylation inhibitor; searching for allosteric effects via QSAR)
RN 198961-42-1 HCAPLUS
CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:658094 HCAPLUS
DOCUMENT NUMBER: 137:185509
TITLE: Preparation of 4-phenylaminoquinazoline derivatives as inhibitors of tyrosine-specific protein kinase
INVENTOR(S): Kitano, Yasunori; Kawahara, Eiji; Suzuki, Tsuyoshi; Abe, Daisuke; Nakajou, Masahiro; Ueda, Naoko
PATENT ASSIGNEE(S): Mitsubishi Pharma Corporation, Japan
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066445	A1	20020829	WO 2002-JP1575	20020221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2442742	AA	20020829	CA 2002-2442742	20020221
EP 1369418	A1	20031210	EP 2002-700688	20020221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1492860	A	20040428	CN 2002-805260	20020221
US 2004116422	A1	20040617	US 2003-468788	20030821

PRIORITY APPLN. INFO.:	JP 2001-45827	A	20010221
	JP 2001-353525	A	20011119
	WO 2002-JP1575	W	20020221

OTHER SOURCE(S): MARPAT 137:185509
GI

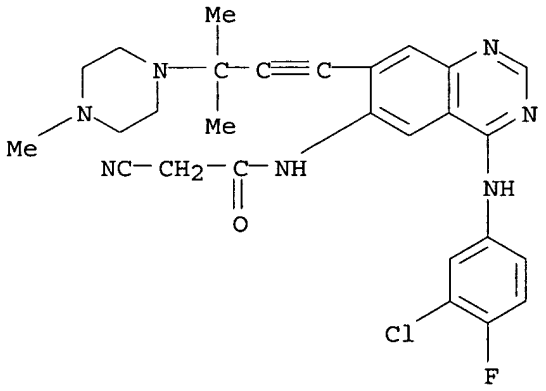
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. represented by the following general formula (I) or pharmaceutically acceptable salts thereof, hydrates or solvates of the same or mixts. of optically active isomers, racemic compds. or diastereomers of the same [n = an integer of 0-3; R1 = H, halo, HO, cyano, NO2, CF3, C1-5 alkyl, C1-5 alkoxy, S(O)f-C1-5 alkyl (wherein f = an integer of 0-2), (un)substituted NH2; one of R2 and R2 is R27SO2NH, (R28SO2)2N, C1-5 alkoxy, MeCOCH2CONH, MeSCH2CH2OCONH, or NCCH2CONH, etc. (wherein R27, R28 = optionally morpholino-substituted C1-5 alkyl) and the other one represents Y(CR12R13)mCR8R9C.tplbond.C, Y(CR12R13)mCR8R9CH:CH, Q, Q1 (wherein R8, R9 = H, optionally HO- or C1-5 alkoxy substituted C1-5 alkyl, or CR8 R9 together represent CO or C3-8 cycloalkylene optionally interrupted by O, S, NH, or alkyl-N; Y = H,HO, C1-5 alkoxy, C1-5 alkanoyloxy, etc.; R11, R12 = H, C1-5 alkyl; m = an integer of 0-3; p, q = 2,3; Z = O, S, SO, SO2, CO, optionally substituted NH; p1, p2 = an integer of 1-3; n1 = 0,1; W = H,HO, C1-5 alkoxy, C1-5 alkanoyloxy, CO2H, cyano, di-C1-5 alkyamino, morpholino, etc.)] are prepared These compds. have an excellent protein kinase inhibitory activity specific to tyrosine and, therefore, are usable as drugs, in particular, remedies/preventives for various cancers, diseases caused by arteriosclerosis or psoriasis. Thus, 1-(1,1-dimethyl-2-propynyl)-4-methylpiperazine was treated with 4,4,5,5-tetramethyl-1,3,2-dioxaborane in the presence of PhCl(PPh3)3 in THF/CH2Cl2 at room temperature and coupled with 4-(3-chloro-4-fluorophenylamino)-6-methoxy-7-quinazolinyl triflate (preparation given) in the presence of PdCl2(dppf).CH2Cl2 [dppf = 1,1'-bis(diphenylphosphino)ferrocene] in a mixture of DMF and 2 m aqueous Na2CO3 80° for 1 h to give the title compound (II). II.HCl showed IC50 of 0.82 nM against EGF receptor tyrosine kinase.

IT **451493-67-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylaminoquinazoline derivs. as inhibitors of tyrosine-specific protein kinase for preparation and/or treatment of cancers, diseases caused by arteriosclerosis, or psoriasis)

RN 451493-67-7 HCAPLUS

CN Acetamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-methyl-3-(4-methyl-1-piperazinyl)-1-butynyl]-6-quinazolinyl]-2-cyano- (9CI) (CA INDEX NAME)

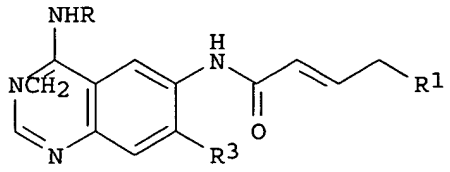


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:487536 HCAPLUS
DOCUMENT NUMBER: 137:63250
TITLE: Quinazoline derivatives as inhibitors of human EFG tyrosine kinase
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Blech, Stefan; Jung, Birgit; Baum, Elke; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050043	A1	20020627	WO 2001-EP14569	20011212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10063435	A1	20020704	DE 2000-10063435	20001220
CA 2432428	AA	20020627	CA 2001-2432428	20011212
AU 2002019174	A5	20020701	AU 2002-19174	20011212
EP 1345910	A1	20030924	EP 2001-271363	20011212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300300	A	20031015	EE 2003-300	20011212
BR 2001016266	A	20040217	BR 2001-16266	20011212
JP 2004516283	T2	20040603	JP 2002-551540	20011212
US 2002173509	A1	20021121	US 2001-23099	20011217
ZA 2003004141	A	20040415	ZA 2003-4141	20030528
NO 2003002726	A	20030616	NO 2003-2726	20030616
BG 107929	A	20050131	BG 2003-107929	20030619
PRIORITY APPLN. INFO.:			DE 2000-10063435 A	20001220
			US 2000-259201P P	20001228
			WO 2001-EP14569 W	20011212

OTHER SOURCE(S): MARPAT 137:63250
GI



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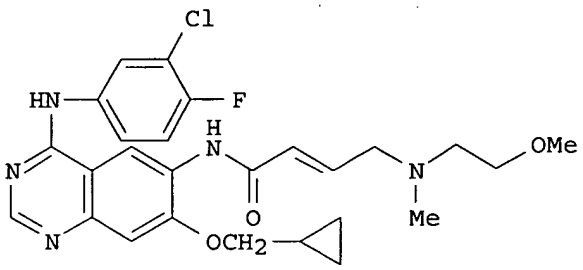


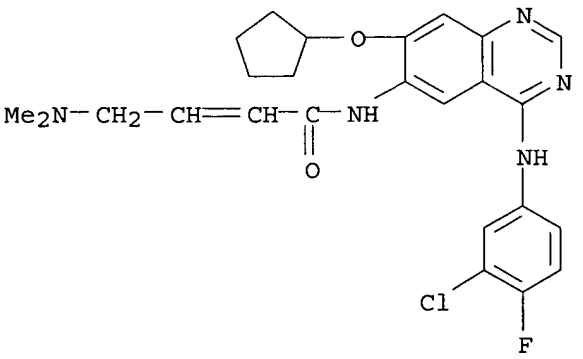
II

AB Quinazoline derivs. I [R = PhCH2, PhCHMe, 3,4-Cl(F)C6H3; R1 = NMeR2, NEt2, NEtCH2CH2OMe, N(CH2CH2OMe)2, morpholino; R2 = Me, Et, CHMe2, cyclopropyl, CH2CH2OMe, 3-tetrahydrofuryl, 2-tetrahydrofurylmethyl, 3-tetrahydrofurylmethyl, 4-tetrahydropyranyl, 4-tetrahydropyranylmethyl; R3 = cyclopropylmethoxy, cyclobutyloxy, cyclopentyloxy, 3-tetrahydrofuranyloxy, 2-tetrahydrofuranylmethoxy, 3-tetrahydrofuranylmethoxy, 4-tetrahydropyranyloxy, 4-tetrahydropyranylmethoxy] were prepared for use as inhibitors of signal transduction caused by human EFG receptor tyrosine kinase. They are useful in the treatment of tumoral diseases, diseases of the lung and the respiratory tract, the gastrointestinal tract, and the gallbladder and bile ducts. Thus, the quinazoline II was prepared by converting bromocrotonic acid to its chloride, and reaction with 4-[(3-chloro-4-fluorophenyl)amino]-6-amino-7-cyclopropylmethoxyquinazoline, followed by MeNHCH2CH2OMe. II had an IC50 against human EFG receptor kinase of 0.7 nM.

IT **439081-10-4P 439081-11-5P 439081-13-7P**
439081-18-2P 439081-30-8P 439081-40-0P
439081-41-1P 439081-42-2P 439081-48-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

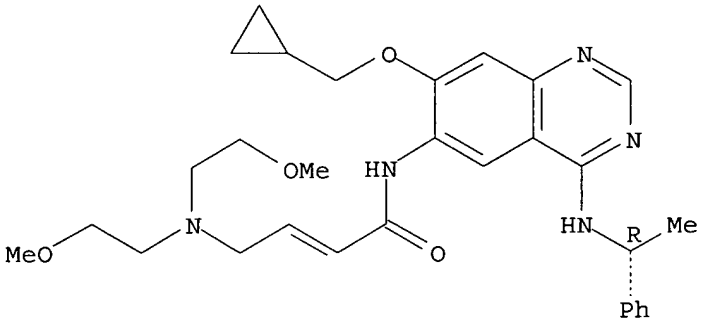
RN 439081-10-4 HCAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



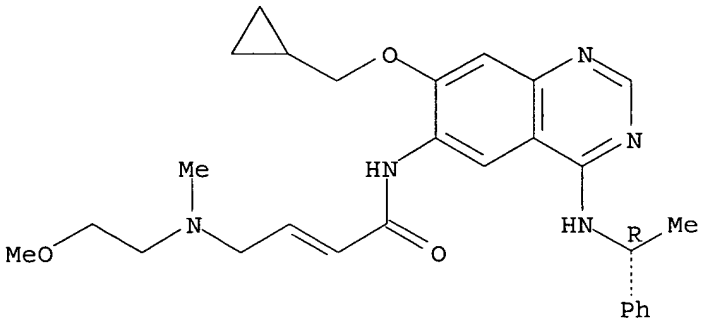
RN 439081-11-5 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-13-7 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

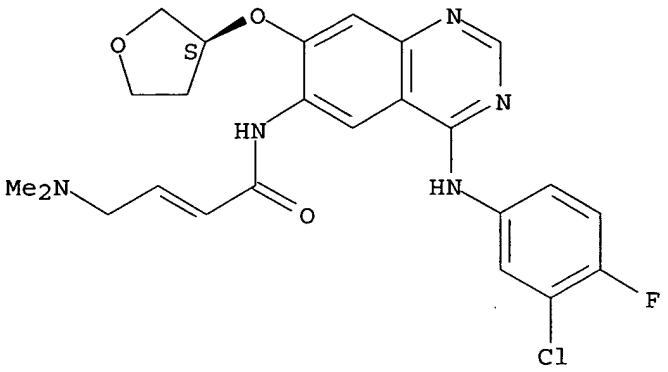
Absolute stereochemistry.
Double bond geometry unknown.



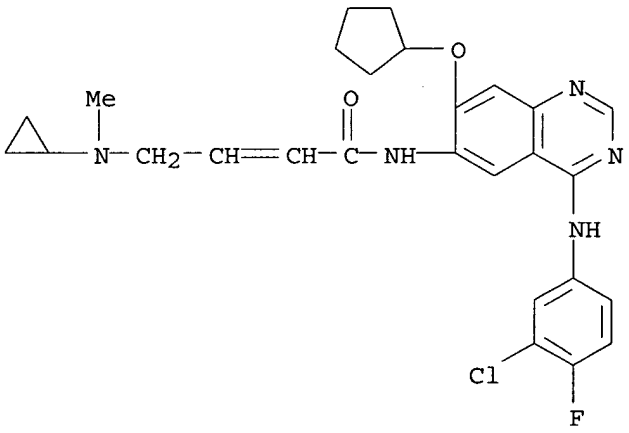
RN 439081-18-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-

furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

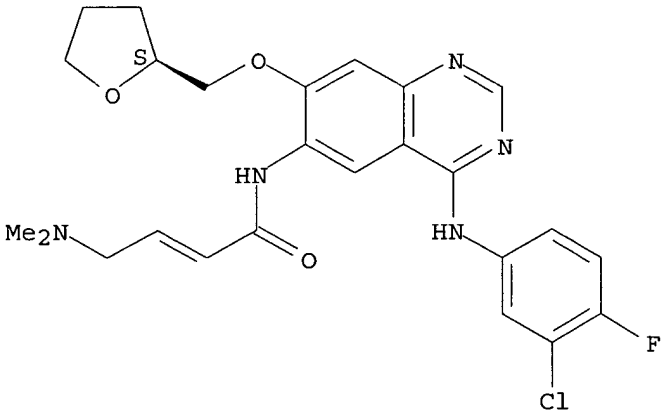


RN 439081-30-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)



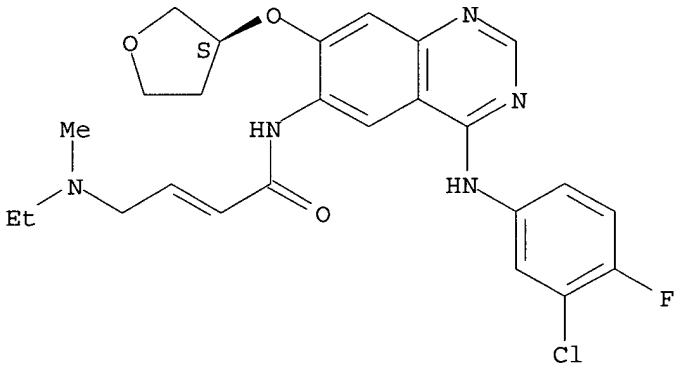
RN 439081-40-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



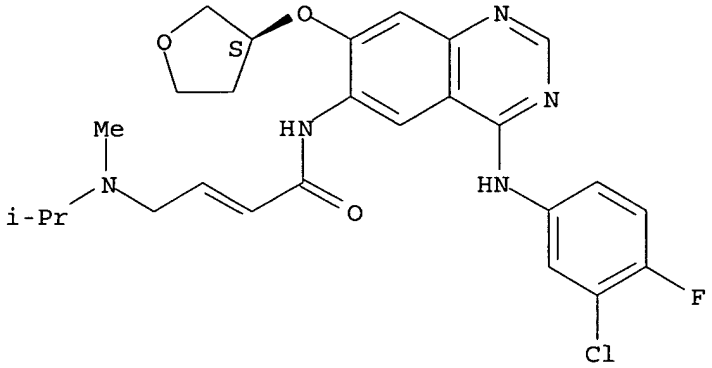
RN 439081-41-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(ethylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

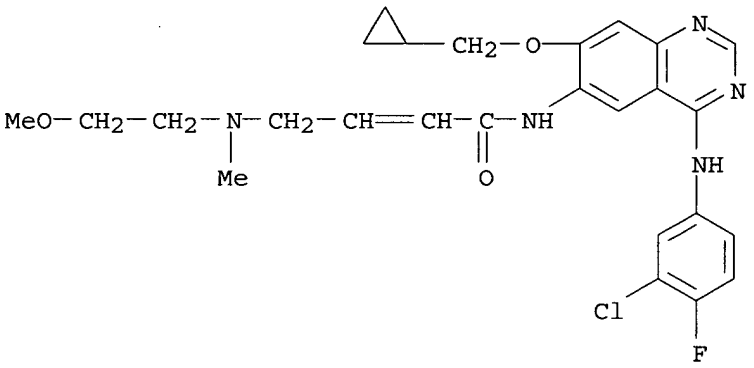


RN 439081-42-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

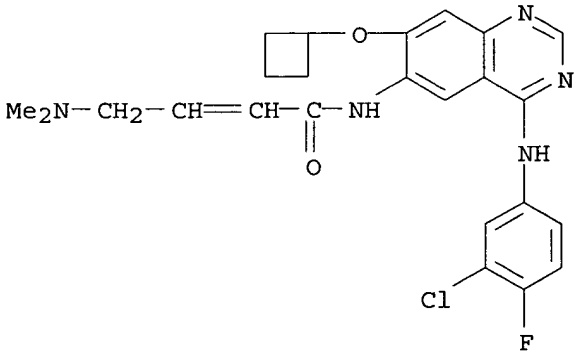
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-48-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

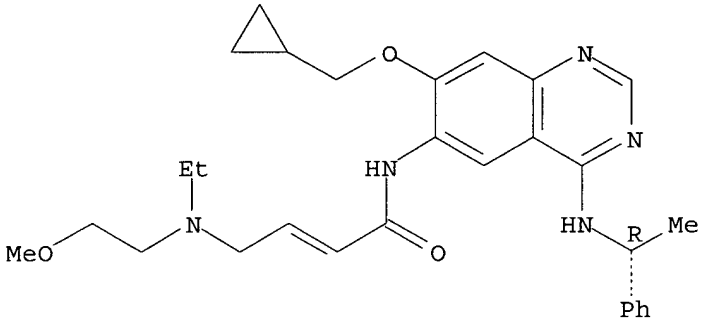


IT **439081-09-1P 439081-12-6P 439081-14-8P**
439081-15-9P 439081-16-0P 439081-17-1P
439081-19-3P 439081-20-6P 439081-21-7P
439081-22-8P 439081-23-9P 439081-24-0P
439081-26-2P 439081-27-3P 439081-28-4P
439081-29-5P 439081-31-9P 439081-32-0P
439081-33-1P 439081-34-2P 439081-35-3P
439081-36-4P 439081-38-6P 439081-39-7P
439081-44-4P 439081-45-5P 439081-46-6P
439081-47-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)
RN 439081-09-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



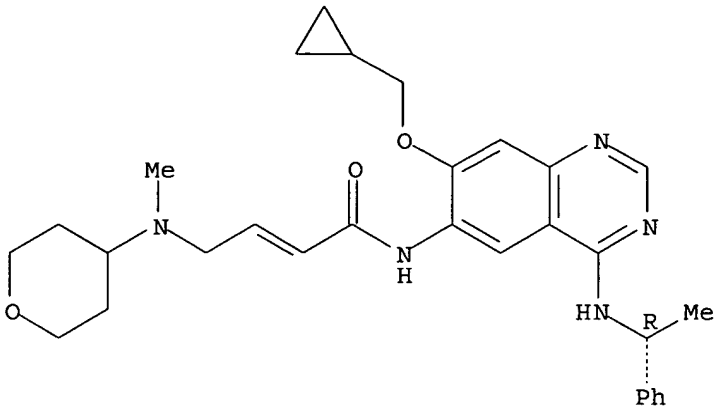
RN 439081-12-6 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



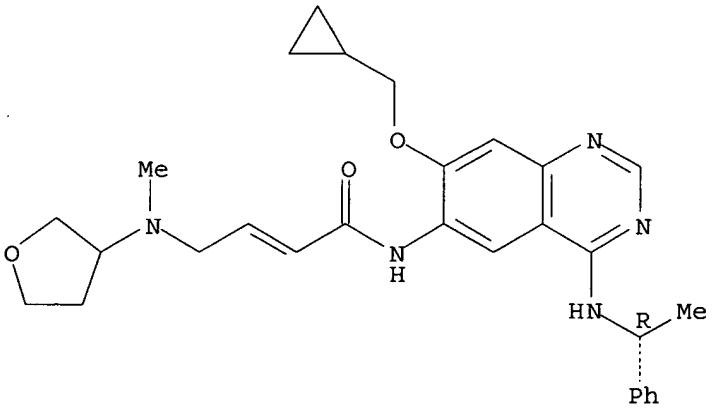
RN 439081-14-8 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

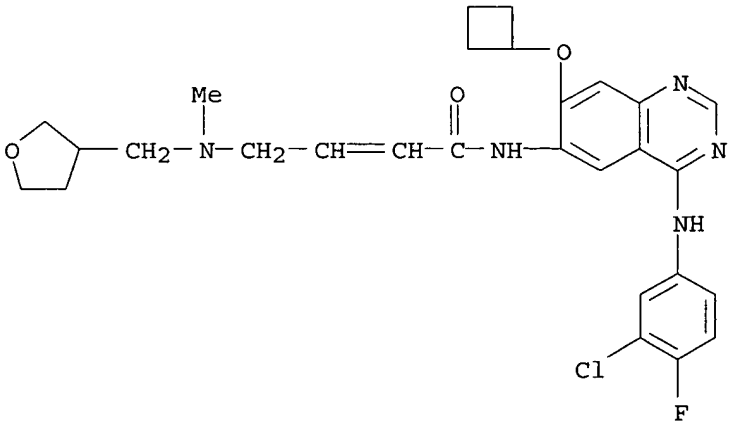


RN 439081-15-9 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-3-furanyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

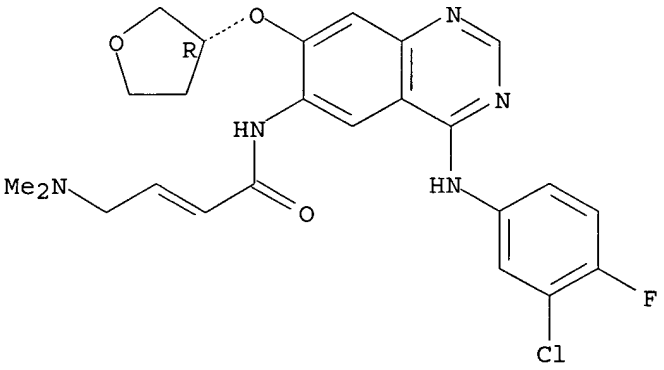


RN 439081-16-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-3-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

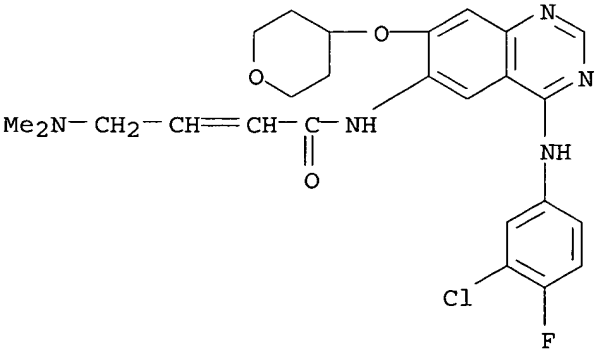


RN 439081-17-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

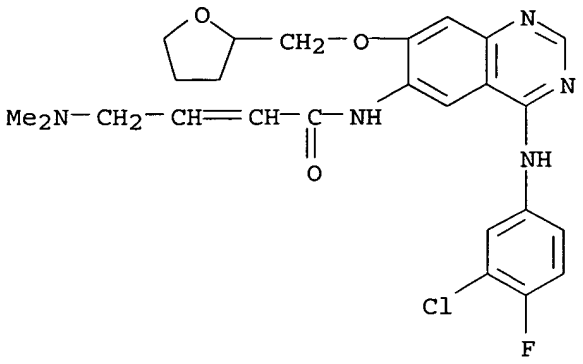
Absolute stereochemistry.
Double bond geometry unknown.



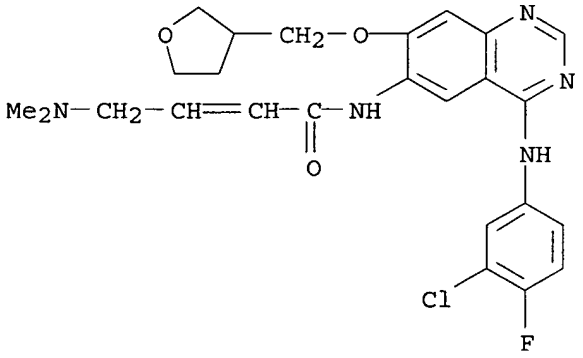
RN 439081-19-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



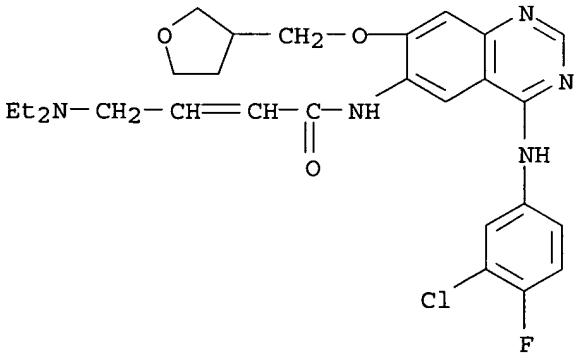
RN 439081-20-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 439081-21-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

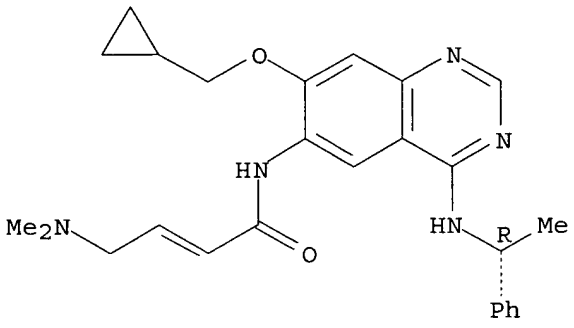


RN 439081-22-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

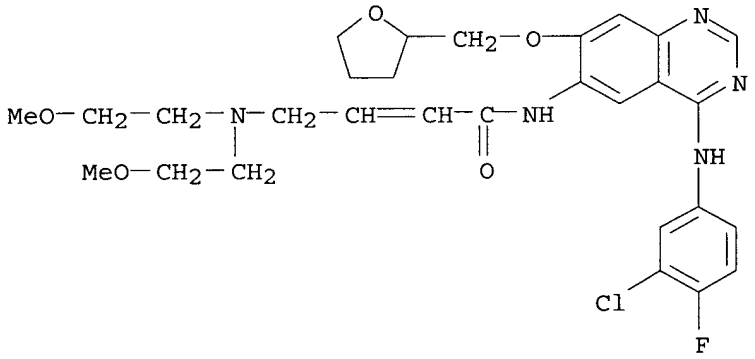


RN 439081-23-9 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

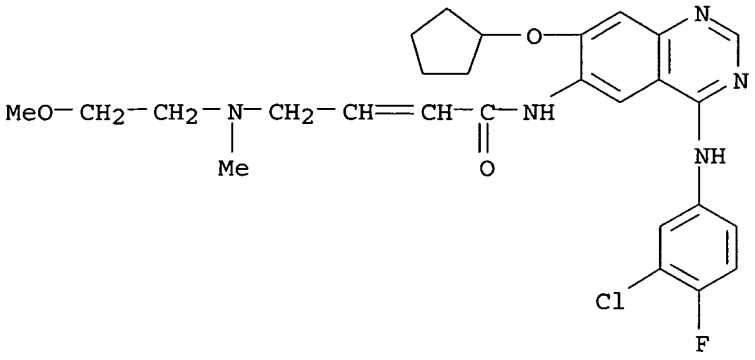
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-24-0 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

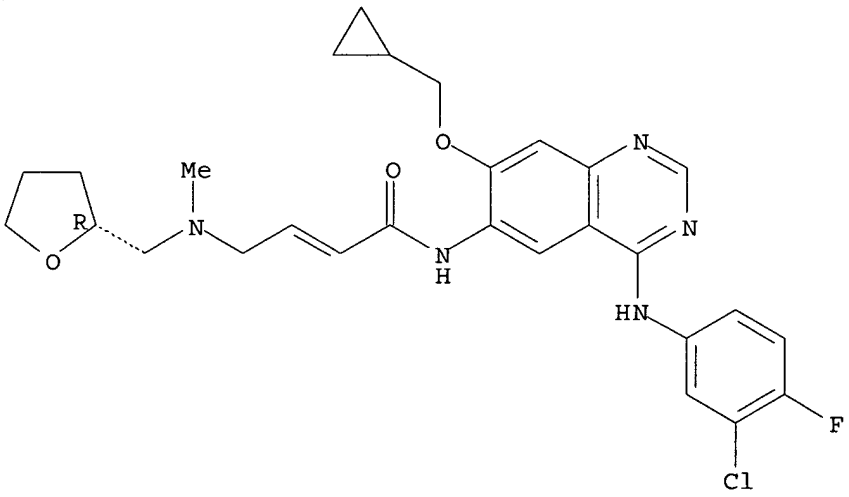


RN 439081-26-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



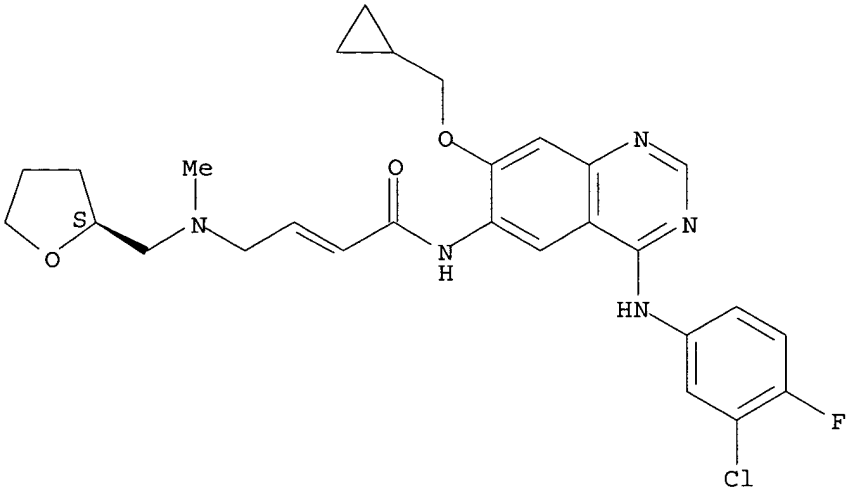
RN 439081-27-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[[(2R)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



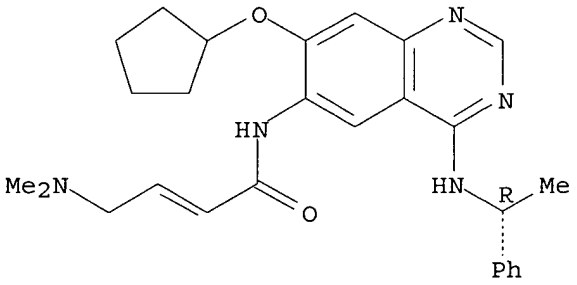
RN 439081-28-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[[(2S)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

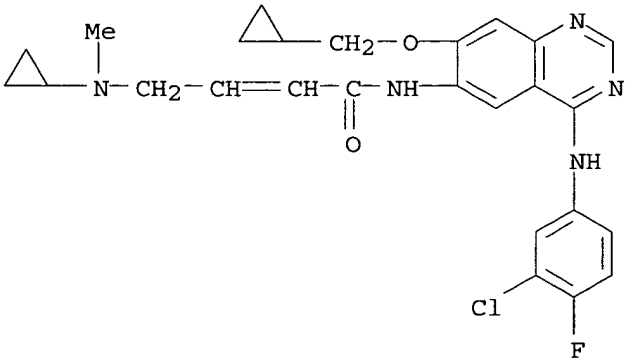


RN 439081-29-5 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopentyloxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

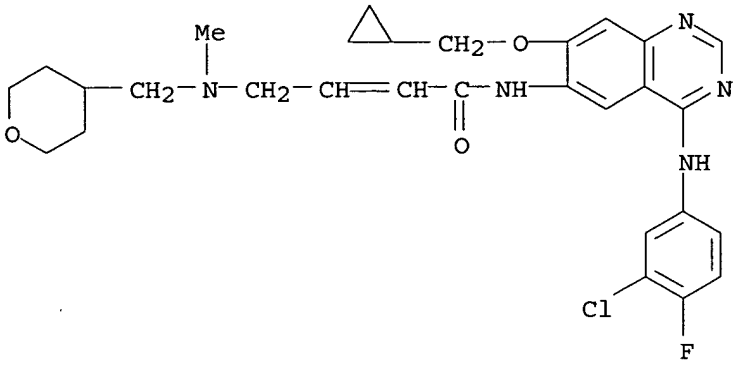
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-31-9 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)

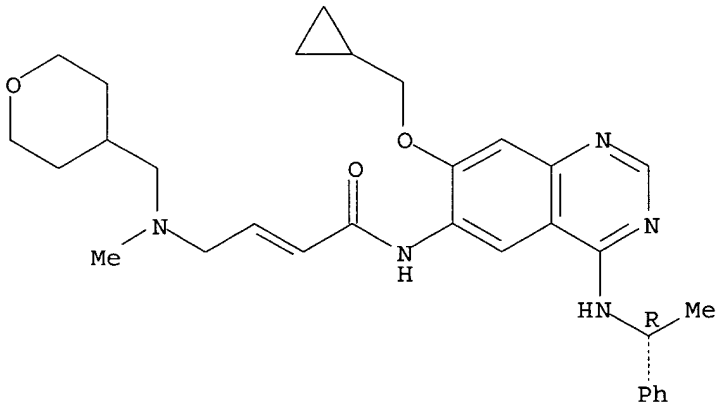


RN 439081-32-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-2H-pyran-4-yl)methyl]amino]- (9CI) (CA INDEX NAME)



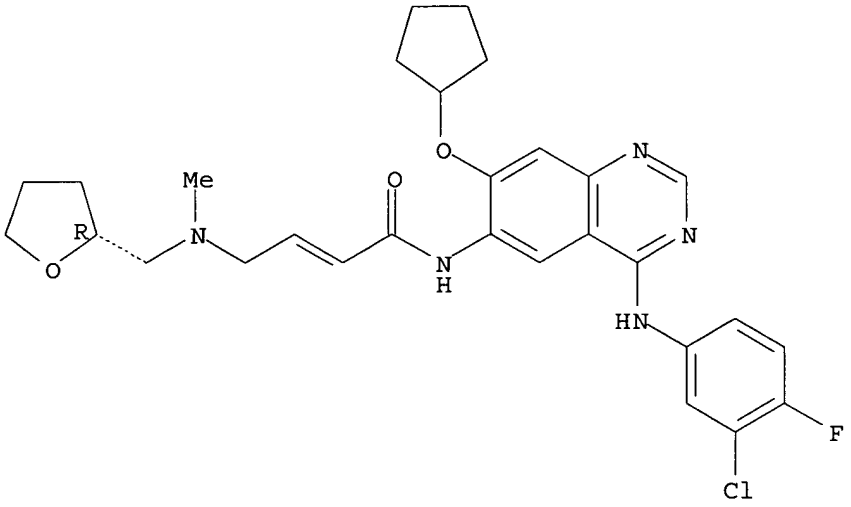
RN 439081-33-1 HCAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl[(tetrahydro-2H-pyran-4-yl)methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



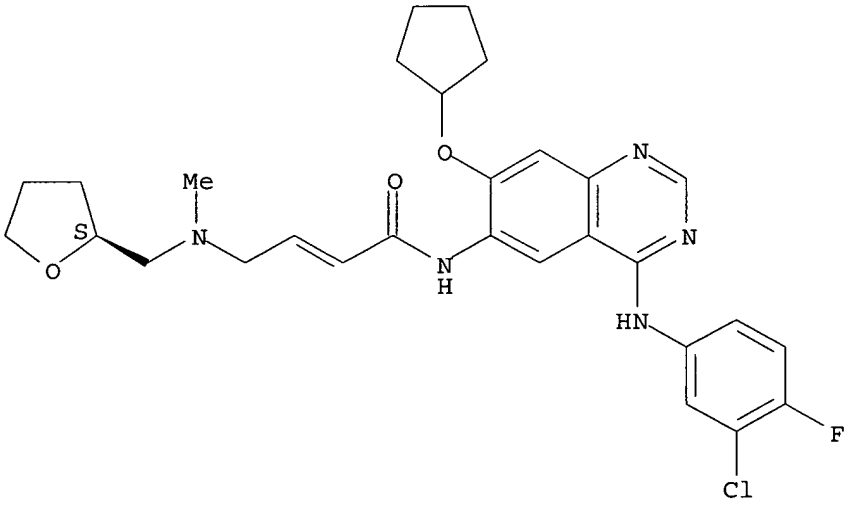
RN 439081-34-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl[[(2R)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

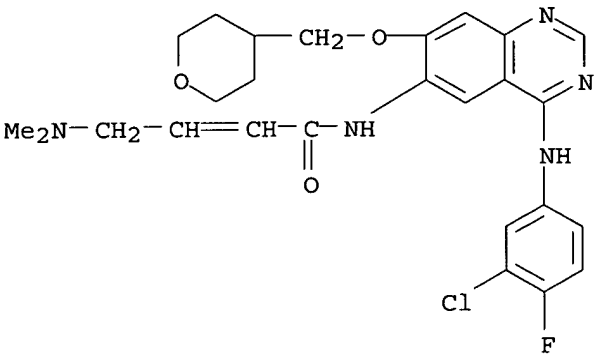


RN 439081-35-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl[[(2S)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

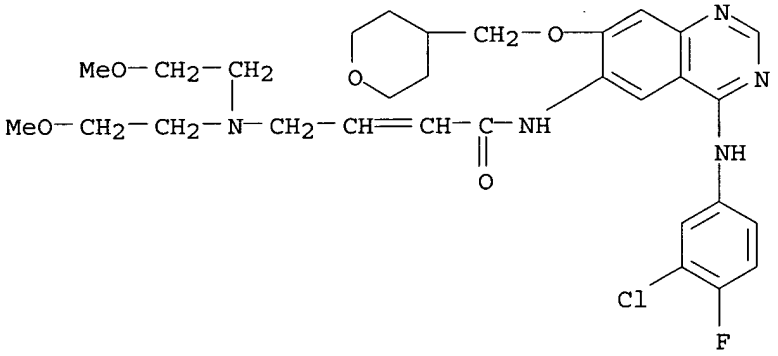
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-36-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

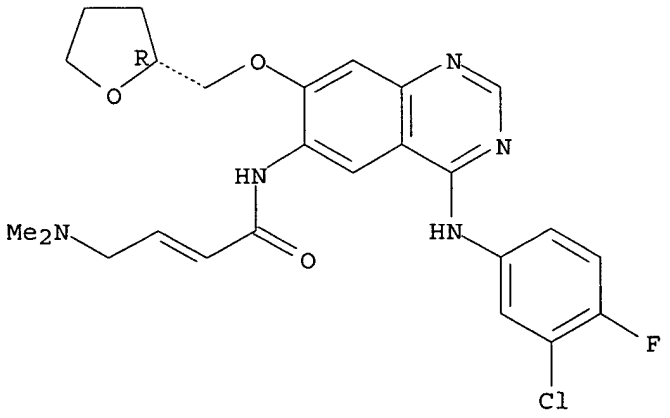


RN 439081-38-6 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

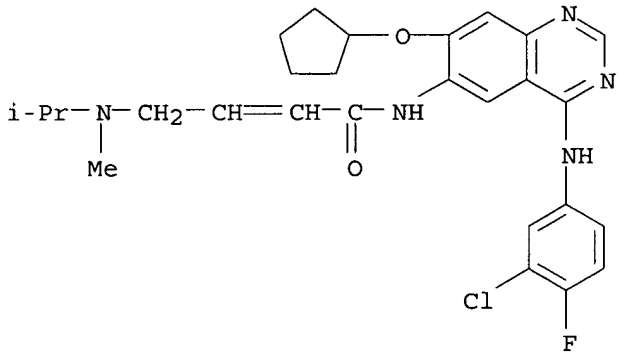


RN 439081-39-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

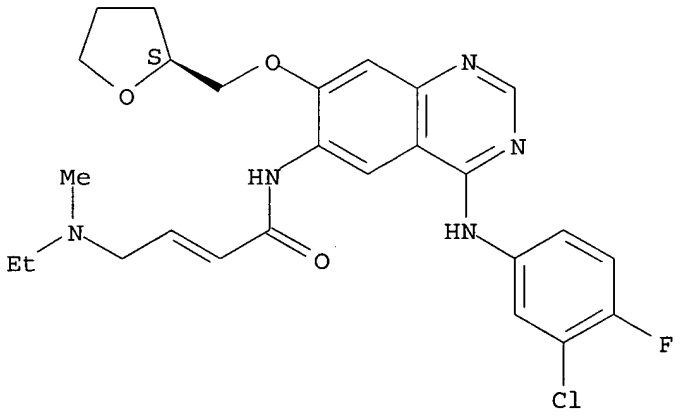


RN 439081-44-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



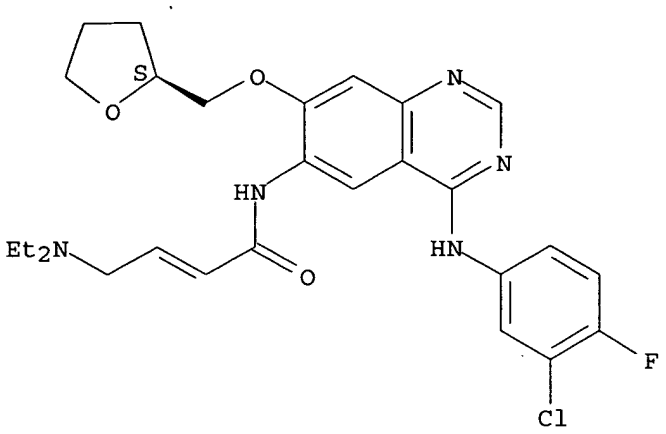
RN 439081-45-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(ethylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



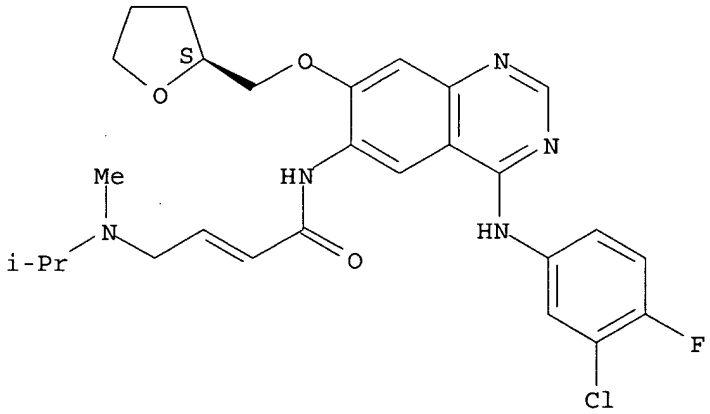
RN 439081-46-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-47-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:171892 HCAPLUS
DOCUMENT NUMBER: 136:216762
TITLE: Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018376	A1	20020307	WO 2001-EP9536	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042062	A1	20020307	DE 2000-10042062	20000826
AU 2001095482	A5	20020313	AU 2001-95482	20010818
CA 2417907	AA	20030130	CA 2001-2417907	20010818
EP 1315720	A1	20030604	EP 2001-976108	20010818
EP 1315720	B1	20050706		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507538	T2	20040311	JP 2002-523891	20010818
AT 299143	E	20050715	AT 2001-976108	20010818
US 2002115675	A1	20020822	US 2001-934631	20010822
US 6740651	B2	20040525		

PRIORITY APPLN. INFO.:	DE 2000-10042062	A	20000826
	US 2000-230542P	P	20000905
	WO 2001-EP9536	W	20010818

OTHER SOURCE(S): MARPAT 136:216762

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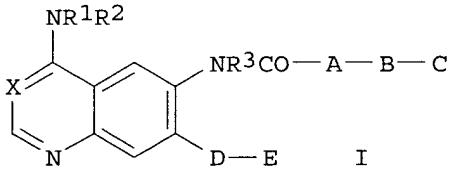


I

AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 = (substituted) Ph, PhCH2, 1-phenylethyl; R3 = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = (substituted) alkenyl, alkenylcarbonyl, etc.; C = (substituted) 2-oxomorpholin-4-yl, etc; D = oxyalkenyl, O; E = (substituted) amino, alkenylimino, imidazolyl, cycloalkyl; or DE = H, (substituted) alkoxy, etc.], were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(ethoxycarbonylmethyl)-N-((R)-2-hydroxy-3-methoxypropyl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline (preparation given) and MeSO2OH in MeCN were stirred for 4 h under reflux to give 69% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[(R)-2-methoxymethyl-6-oxomorpholin-4-yl]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 2 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

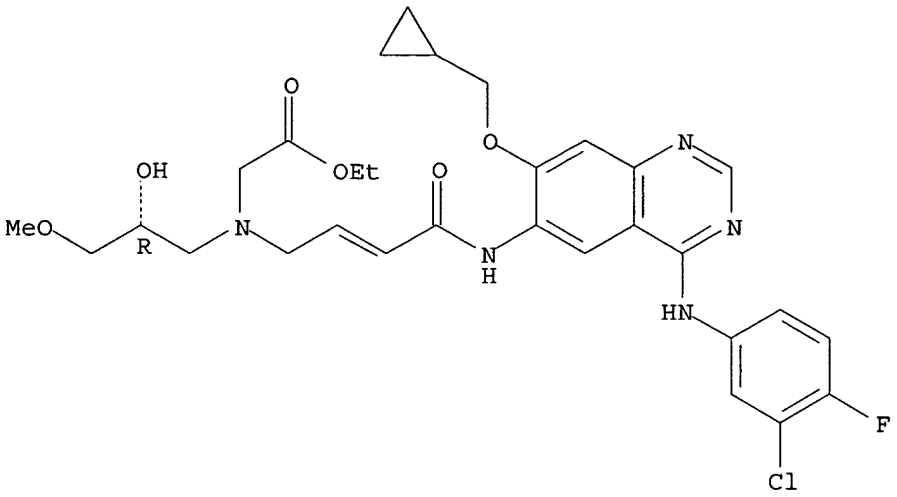
IT **402569-87-3P 402569-89-5P 402569-90-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (amino)(heterocyclylcarbonylamino)quinazolines as epidermal

growth factor receptor signal transduction inhibitors)

RN 402569-87-3 HCAPLUS

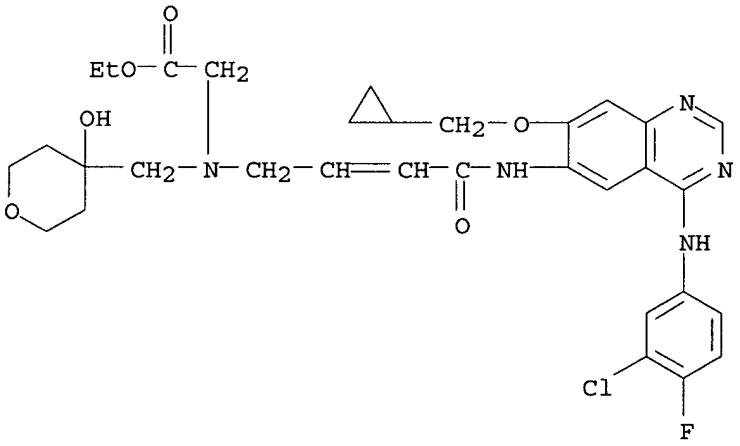
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402569-89-5 HCAPLUS

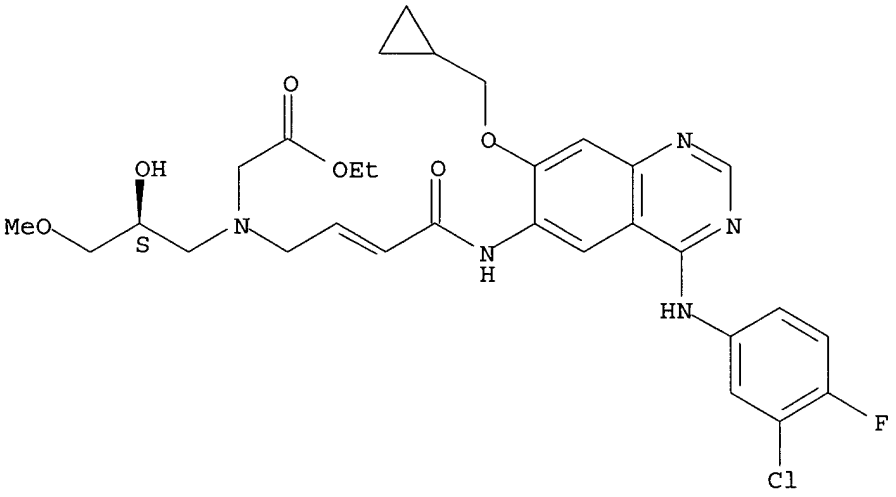
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(tetrahydro-4-hydroxy-2H-pyran-4-yl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 402569-90-8 HCAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



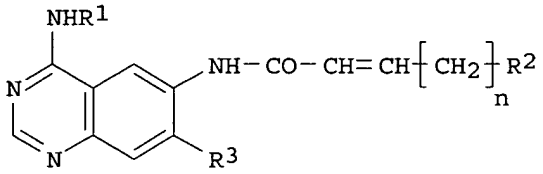
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:171889 HCAPLUS
DOCUMENT NUMBER: 136:232315
TITLE: Preparation of 4-amino-6-vinylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018373	A1	20020307	WO 2001-EP9537	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042060	A1	20020307	DE 2000-10042060	20000826
US 2002077330	A1	20020620	US 2001-929931	20010815
US 6653305	B2	20031125		
CA 2417050	AA	20020307	CA 2001-2417050	20010818
AU 2001084021	A5	20020313	AU 2001-84021	20010818
EP 1315717	A1	20030604	EP 2001-962953	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

JP 2004517048	T2	20040610	JP 2002-523888		20010818
PRIORITY APPLN. INFO.:			DE 2000-10042060	A	20000826
			US 2000-230389P	P	20000906
			WO 2001-EP9537	W	20010818

OTHER SOURCE(S): MARPAT 136:232315
GI



I

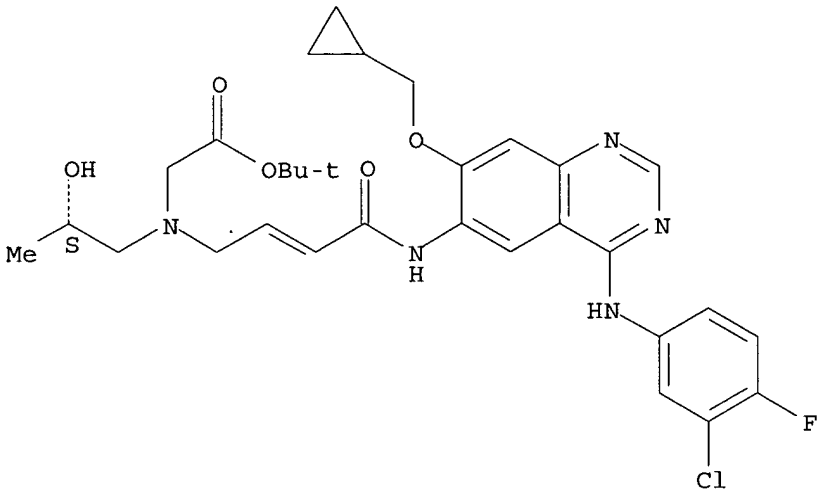
AB Title compds. [I; R1 = PhCH2, 1-phenylethyl, (substituted) Ph; R2 = N-[(1,3-dioxolan-2-yl)methyl]methylamino, (substituted) R4OCOCH2NCH2CH2OH, 2-oxomorpholin-4-yl; R4 = H, alkyl; R3 = H, (alkoxy)alkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; n = 1-3], were prepared Thus, a mixture of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-cyclopropylmethoxyquinazoline (preparation given) and disopropylethylamine in THF was dropwise treated under ice-cooling with BrCH2CH:CHCO2Cl (preparation given) in CH2Cl2 followed by stirring for 1 h under ice-cooling and for 2 h at room temperature and addition of (S)-(2-hydroxypropylamino)acetic acid tert-Bu ester in CH2Cl2 to give after stirring over night at room temperature and stirring for 5 h at 60° 64% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(tert-butyloxycarbonylmethyl)-N-((S)-2-hydroxyprop-1-yl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.02-15 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT **402855-15-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402855-15-6 HCAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

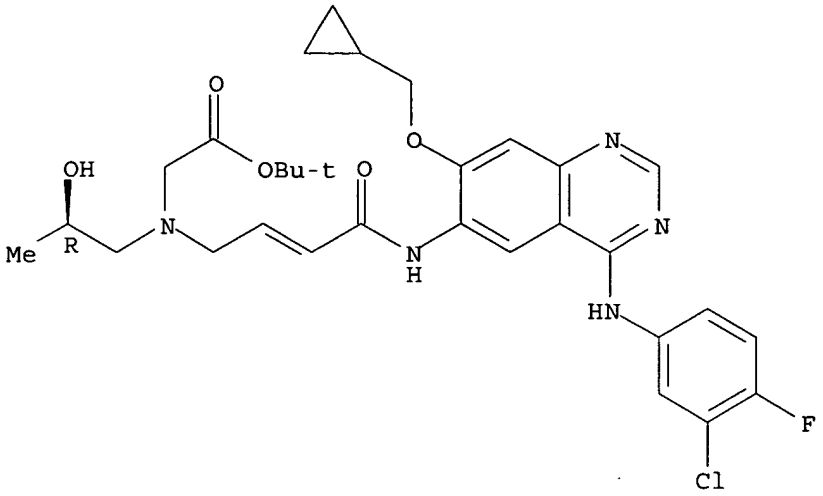


IT **402855-16-7P 402855-17-8P 402855-18-9P**
402855-20-3P 402855-21-4P 402855-26-9P
402855-27-0P 402855-28-1P 402855-31-6P
402855-36-1P 402855-37-2P 402855-39-4P
402855-40-7P 402855-41-8P 402855-42-9P
402855-43-0P 402855-44-1P 402855-45-2P
402855-46-3P 402855-49-6P 402855-50-9P
402855-51-0P 402855-74-7P 402855-75-8P
402855-76-9P 402855-77-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

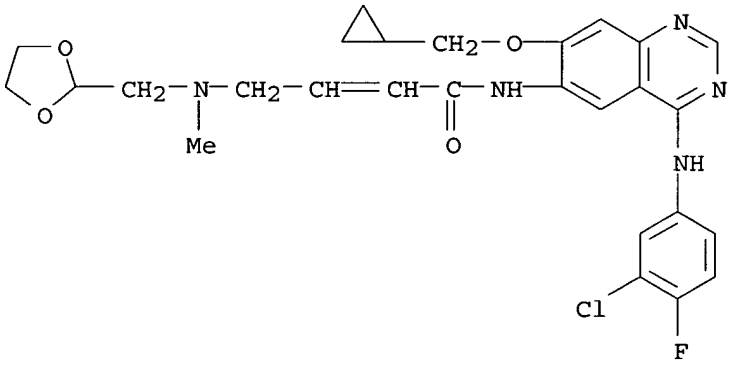
RN 402855-16-7 HCAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

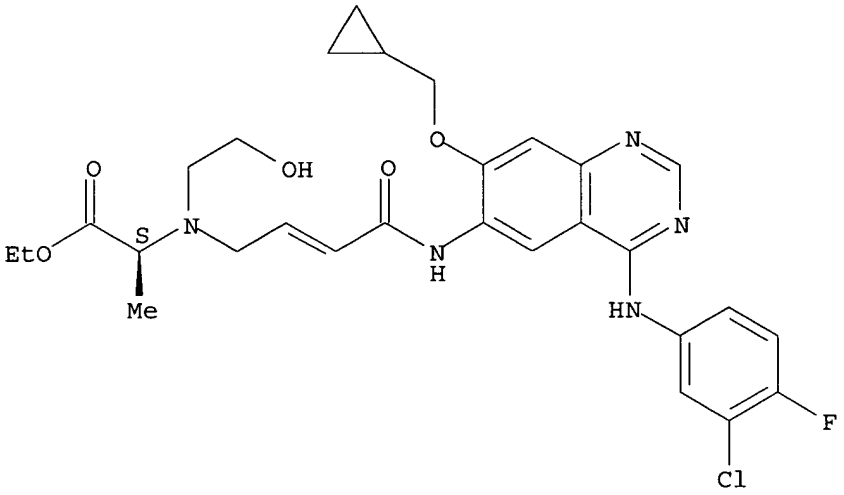


RN 402855-17-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(1,3-dioxolan-2-ylmethyl)methylamino]- (9CI) (CA INDEX NAME)



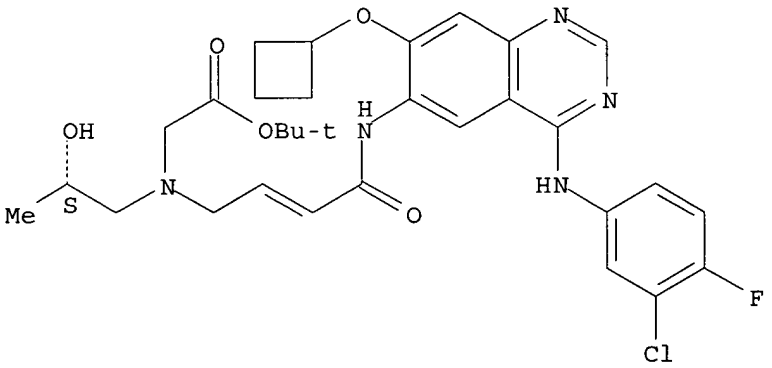
RN 402855-18-9 HCAPLUS
CN L-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



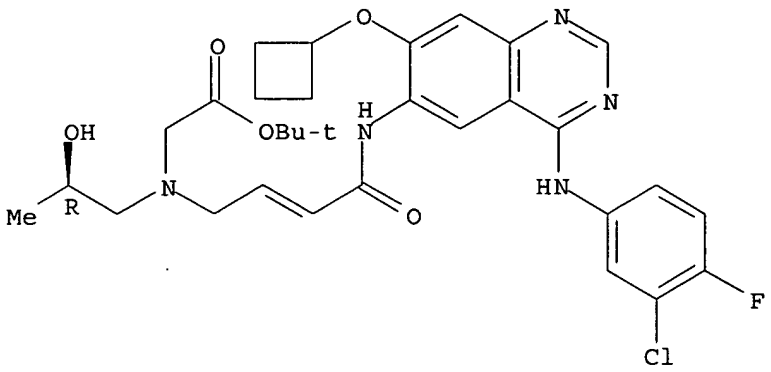
RN 402855-20-3 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



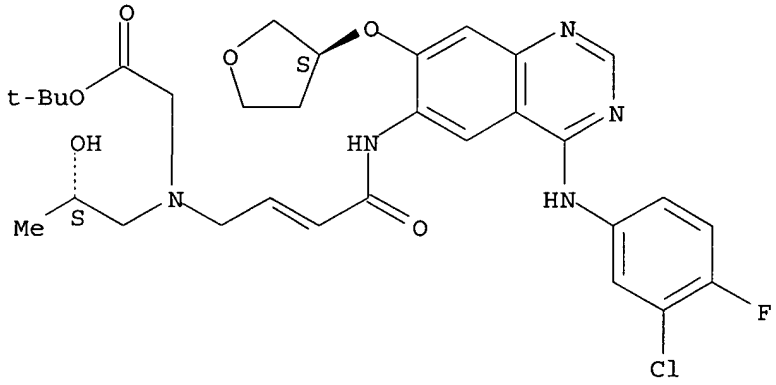
RN 402855-21-4 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



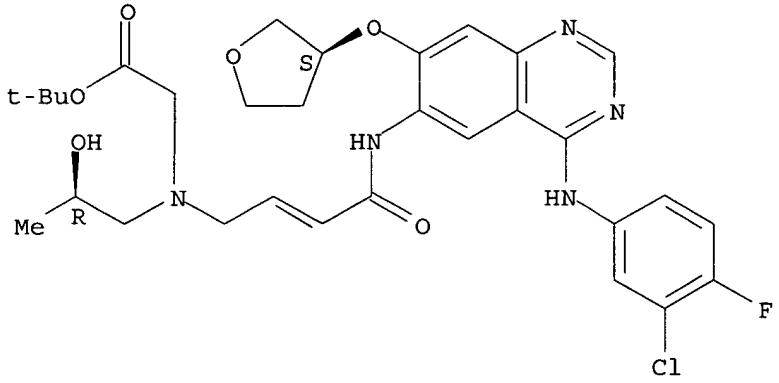
RN 402855-26-9 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



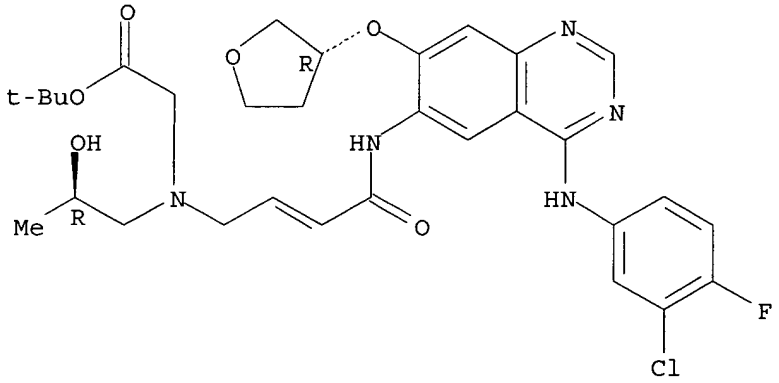
RN 402855-27-0 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

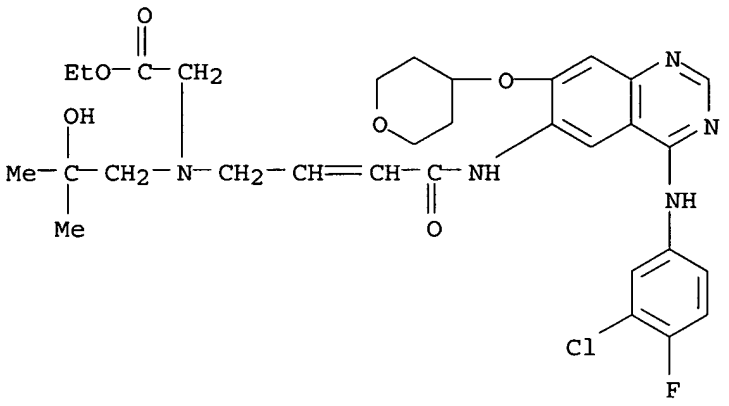


RN 402855-28-1 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

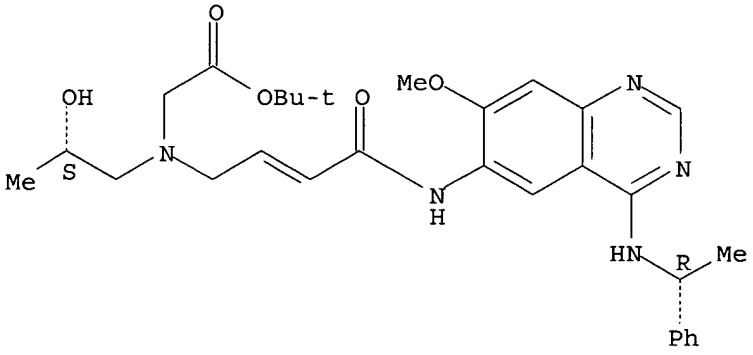


RN 402855-31-6 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)-, ethyl ester (9CI) (CA INDEX NAME)



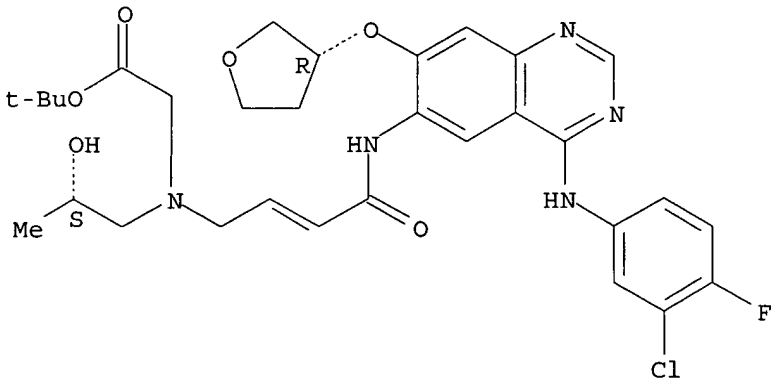
RN 402855-36-1 HCAPLUS
CN Glycine, N-[(2S)-2-hydroxypropyl]-N-[4-[[7-methoxy-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



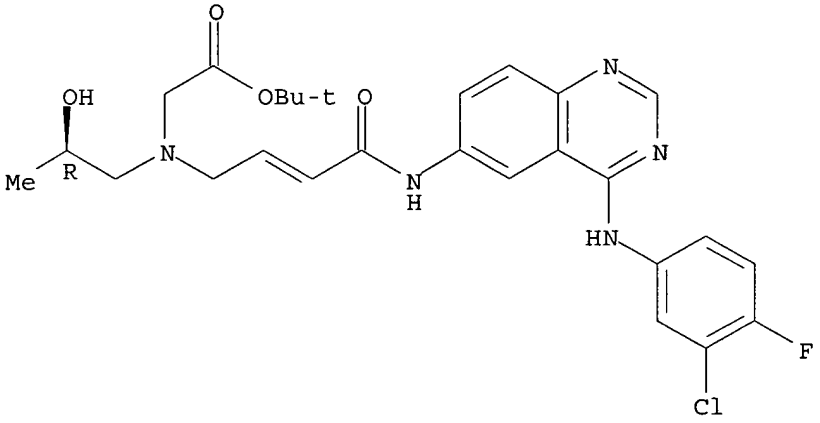
RN 402855-37-2 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



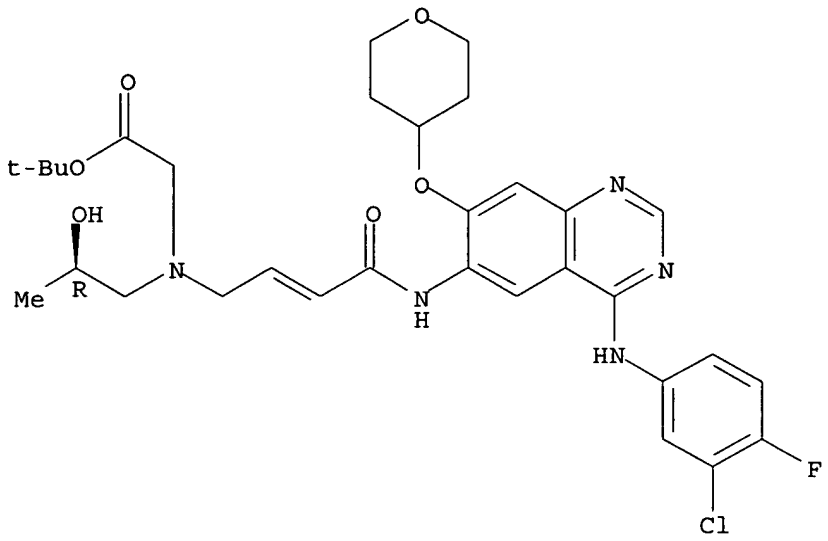
RN 402855-39-4 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



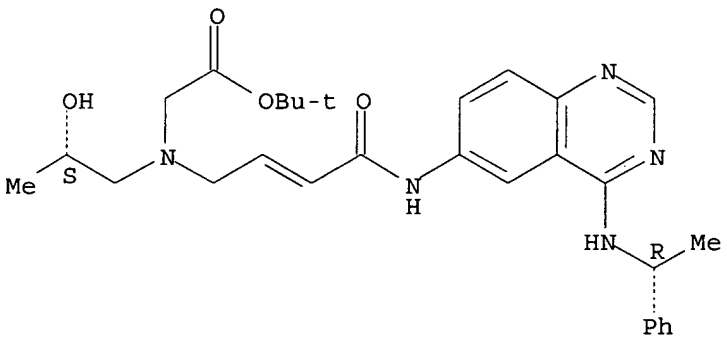
RN 402855-40-7 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



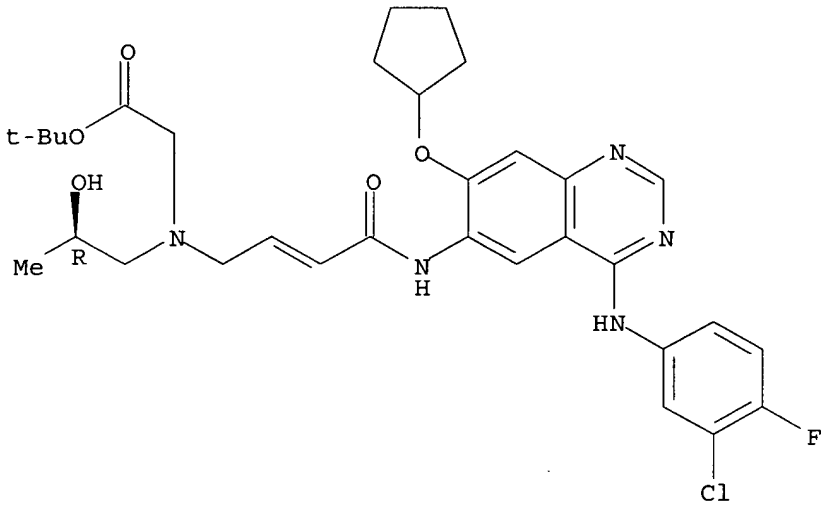
RN 402855-41-8 HCAPLUS
CN Glycine, N-[(2S)-2-hydroxypropyl]-N-[4-oxo-4-[[4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



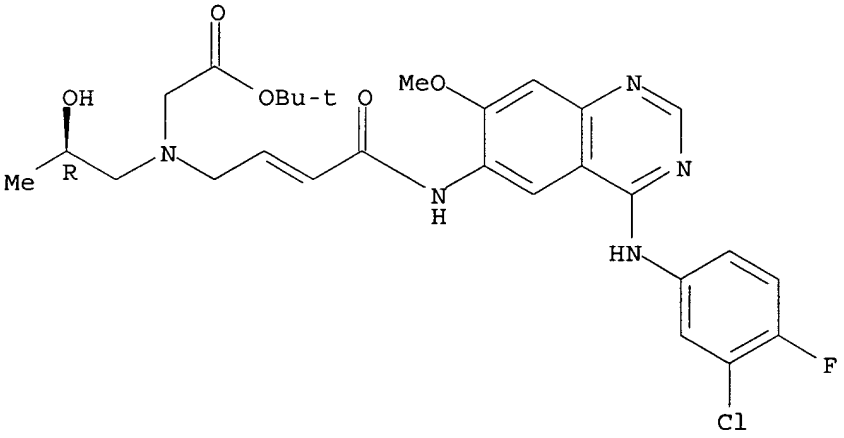
RN 402855-42-9 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



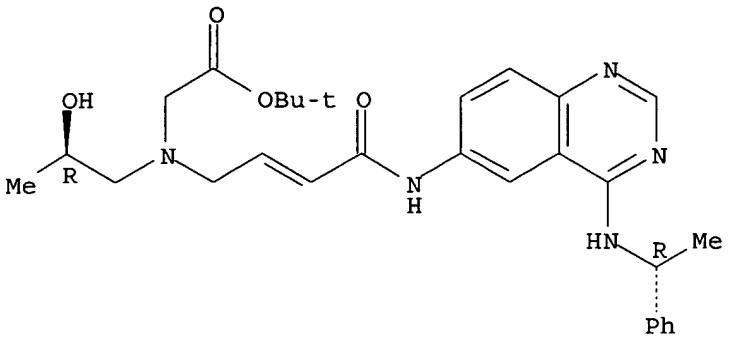
RN 402855-43-0 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



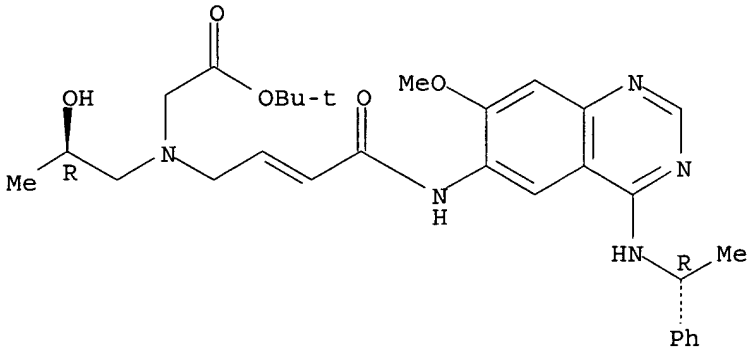
RN 402855-44-1 HCAPLUS
CN Glycine, N-[(2R)-2-hydroxypropyl]-N-[4-oxo-4-[[4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



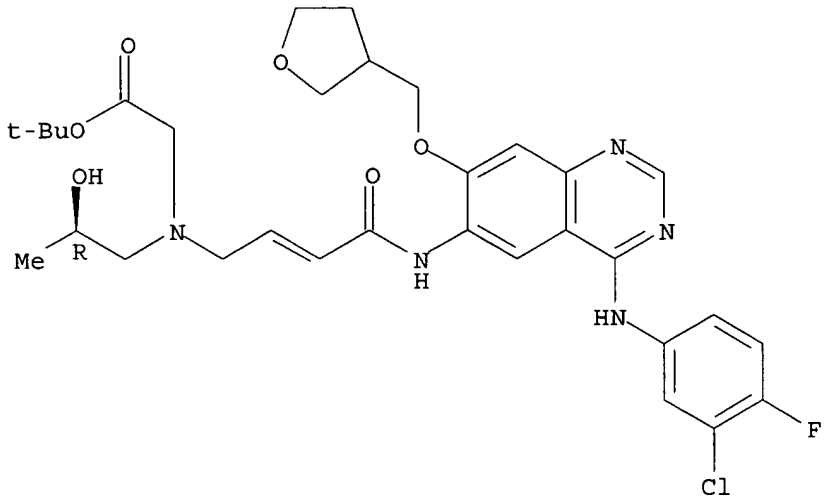
RN 402855-45-2 HCAPLUS
CN Glycine, N-[(2R)-2-hydroxypropyl]-N-[4-[[7-methoxy-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



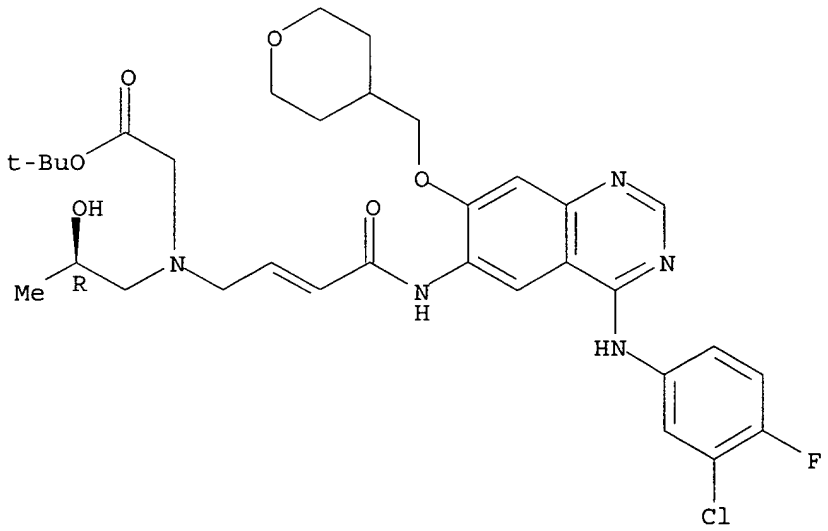
RN 402855-46-3 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



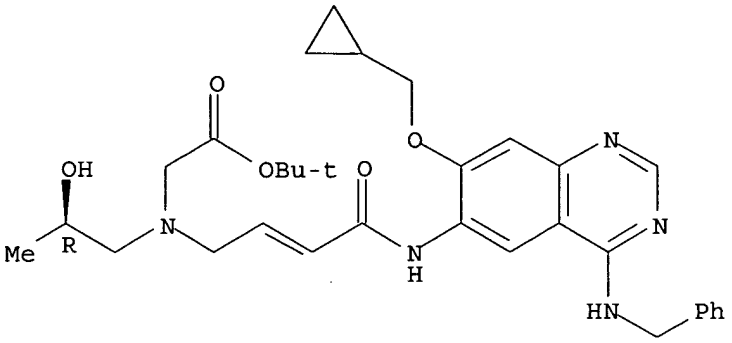
RN 402855-49-6 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



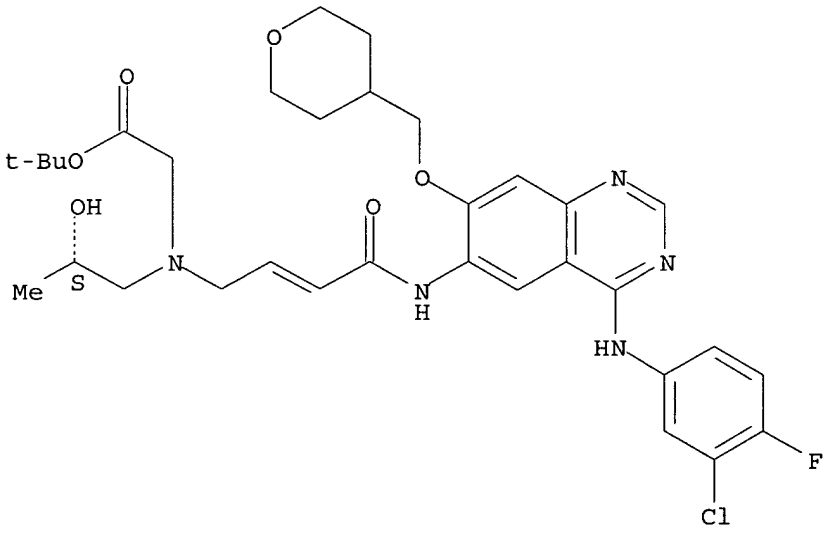
RN 402855-50-9 HCAPLUS
CN Glycine, N-[4-[[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



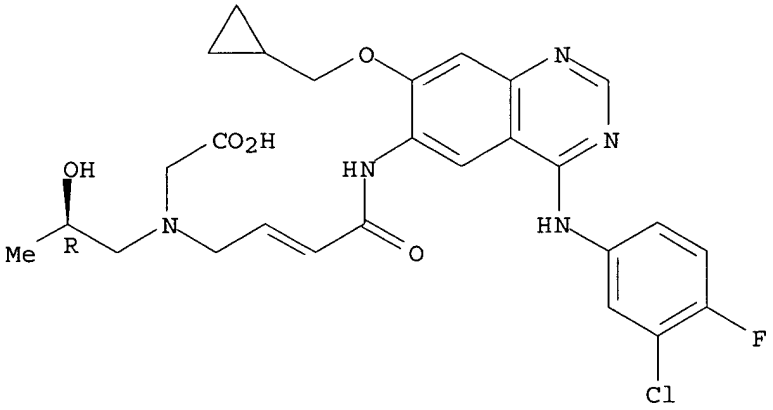
RN 402855-51-0 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

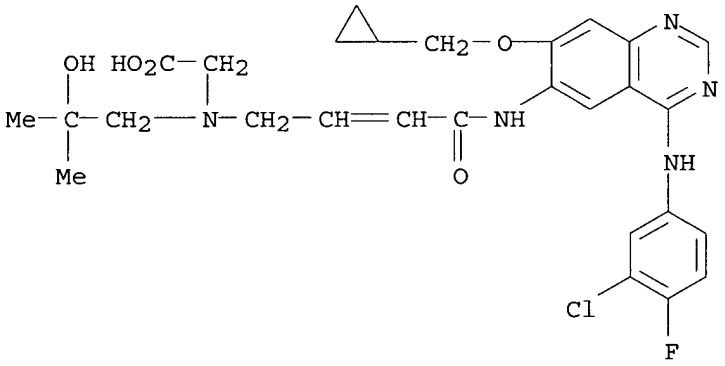


RN 402855-74-7 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

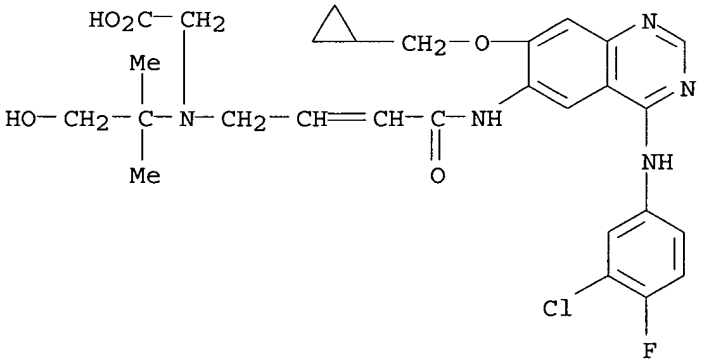
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-75-8 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)- (9CI) (CA INDEX NAME)

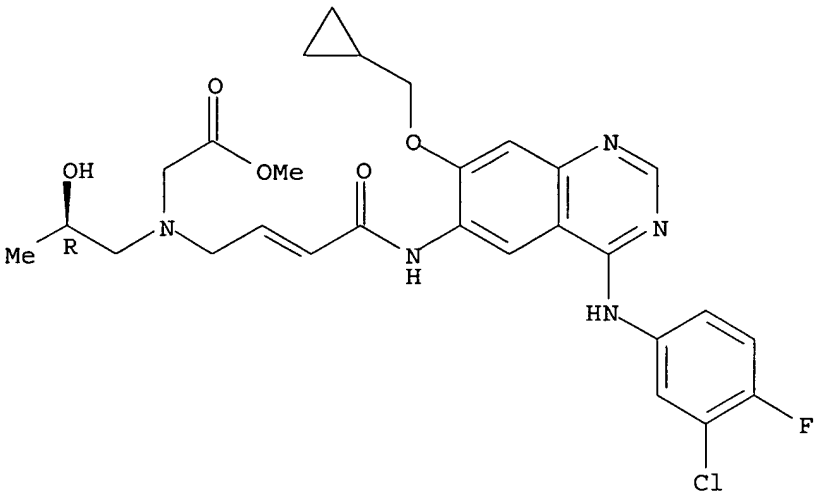


RN 402855-76-9 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



RN 402855-77-0 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

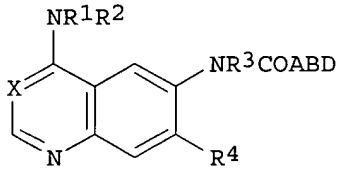
L8 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:762992 HCAPLUS
DOCUMENT NUMBER: 135:303907
TITLE: Preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction.
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10017539	A1	20011011	DE 2000-10017539	20000408
DE 10040525	A1	20020228	DE 2000-10040525	20000818

CA 2403152	AA	20011018	CA 2001-2403152		20010331
AU 2001063831	A5	20011023	AU 2001-63831		20010331
EP 1280798	A1	20030205	EP 2001-938076		20010331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003530395	T2	20031014	JP 2001-575577		20010331
PRIORITY APPLN. INFO.:			DE 2000-10017539	A	20000408
			DE 2000-10040525	A	20000818
			WO 2001-EP3694	W	20010331

OTHER SOURCE(S): MARPAT 135:303907

GI



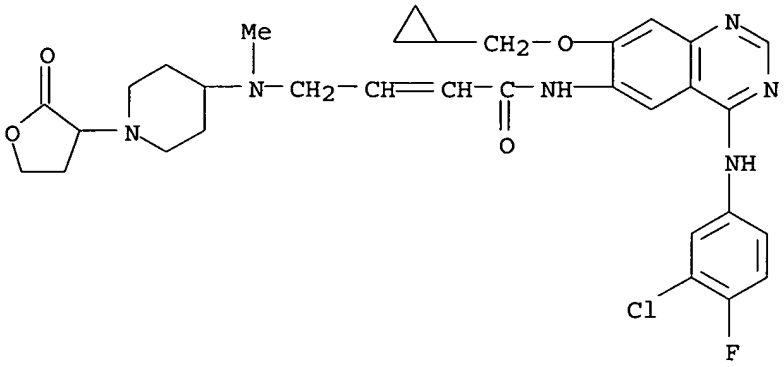
I

AB Title compds. [I; X = NCN, N; R1 = H, alkyl; R2 = (substituted) Ph, PhCH2, PhCH2CH2; R3 = H, alkyl; R4 = H, alkoxy, cycloalkoxy, cycloalkylalkoxy; A = (substituted) vinylene; B = bond, (fluoro)alkylene; D = substituted pyrrolidinyl, piperidinyl, piperazinyl, etc.], were prepared Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-(piperazin-1-yl)-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline (preparation given) in THF was treated with Et3N and then with 3-bromodihydrofuran-2-one in THF under ice cooling followed by stirring for 48 h at room temperature to give 56% 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-[4-(2-oxotetrahydrofuran-3-yl)piperazin-1-yl]-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.05 nM.

IT **367282-07-3P 367282-12-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

RN 367282-07-3 HCAPLUS

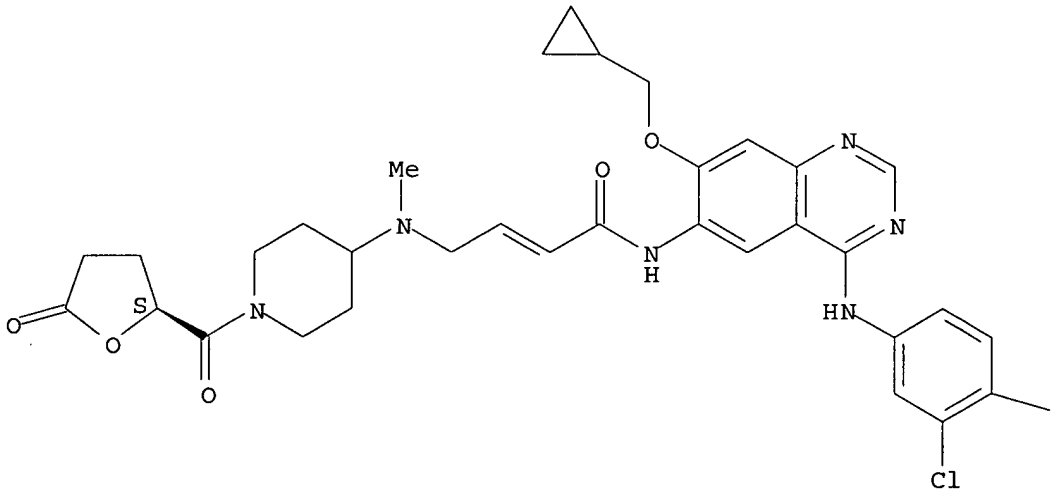
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[1-(tetrahydro-2-oxo-3-furanyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)



RN 367282-12-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[1-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

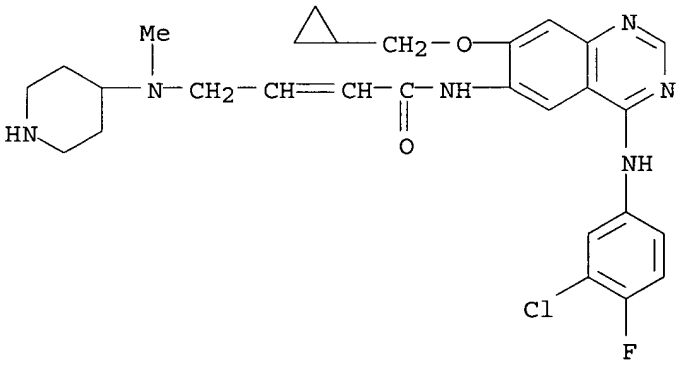
PAGE 1-A



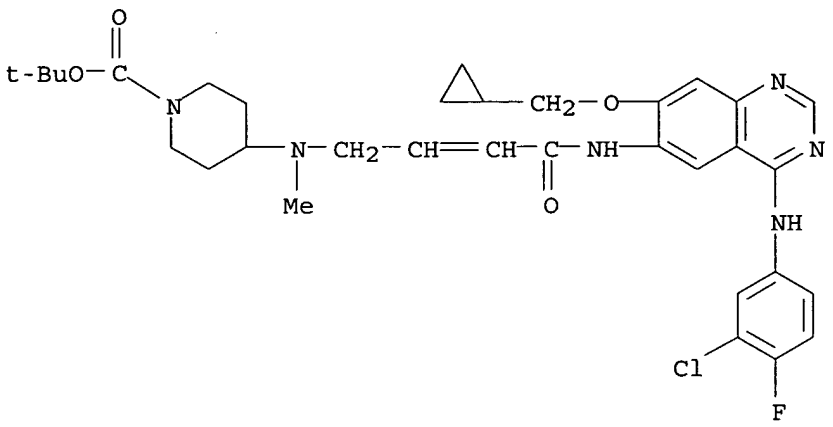
F

IT **367282-36-8P 367282-44-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

RN 367282-36-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(methyl-4-piperidinylamino)- (9CI) (CA INDEX NAME)



RN 367282-44-8 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



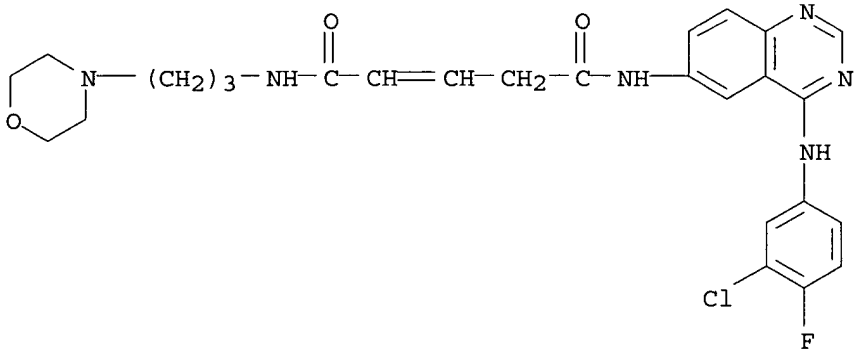
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:516932 HCAPLUS
DOCUMENT NUMBER: 135:313144
TITLE: The 4-anilinoquinazoline class of inhibitors of the erbB family of receptor tyrosine kinases
AUTHOR(S): Denny, William A.
CORPORATE SOURCE: Auckland Cancer Society Research Centre, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, N. Z.
SOURCE: Farmaco (2001), 56(1-2), 51-56
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The erbB family of receptor tyrosine kinase enzymes, and particularly EGFR and HER2/neu, have become important targets for potential anticancer drugs. The substrate protein binding site theor. is the more attractive intracellular target on these enzymes, possessing lower homol. than the ATP site between different receptor kinases. However, a major breakthrough in this field was the discovery that 4-anilinoquinazolines are potent and selective inhibitors, despite binding at the ATP site. The very tight structure-activity relationships shown by these compds. suggested a clearly-defined binding mode, where the quinazoline ring binds in the adenine pocket and the anilino ring binds in an adjacent, unique lipophilic pocket. A unique cysteine (Cys-773) adjacent to the quinazoline binding site has prompted the development of irreversible inhibitors that target this residue. Three 4-anilinoquinazoline analogs (two reversible and one irreversible inhibitor) have been evaluated clin. as anticancer drugs. Data from the most advanced, the reversible inhibitor Iressa, suggest that this class of compds. may be of value in cancer chemotherapy.

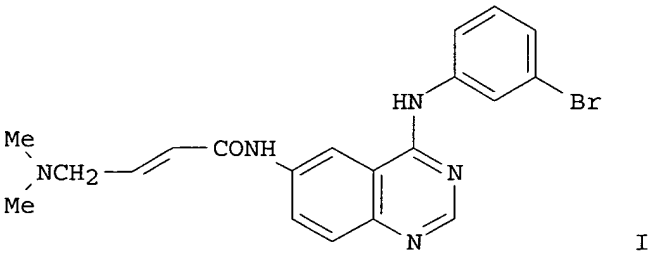
IT **367518-73-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(4-anilinoquinazoline class of inhibitors of erbB family of receptor tyrosine kinases)
RN 367518-73-8 HCAPLUS
CN 2-Pentenediamide, N5-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-

N1-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:514231 HCAPLUS
DOCUMENT NUMBER: 135:251424
TITLE: 6-Substituted-4-(3-bromophenylamino)quinazolines as Putative Irreversible Inhibitors of the Epidermal Growth Factor Receptor (EGFR) and Human Epidermal Growth Factor Receptor (HER-2) Tyrosine Kinases with Enhanced Antitumor Activity
AUTHOR(S): Tsou, Hwei-Ru; Mamuya, Nellie; Johnson, Bernard D.; Reich, Marvin F.; Gruber, Brian C.; Ye, Fei; Nilakantan, Ramaswamy; Shen, Ru; Discafani, Carolyn; DeBlanc, Ronald; Davis, Rachel; Koehn, Frank E.; Greenberger, Lee M.; Wang, Yu-Fen; Wissner, Allan
CORPORATE SOURCE: Wyeth-Ayerst Research A Division of American Home Products, Pearl River, NY, 10965-1215, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(17), 2719-2734
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:251424
GI



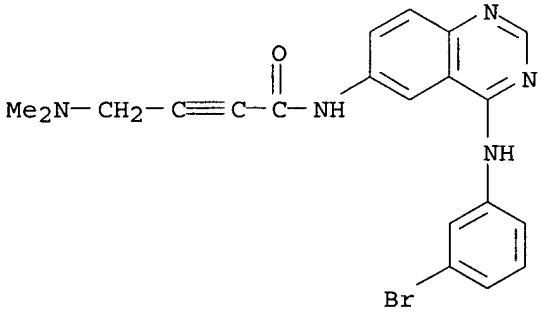
I

AB A series of new 6-substituted-4-(3-bromophenylamino)quinazoline derivs. that may function as irreversible inhibitors of epidermal growth factor

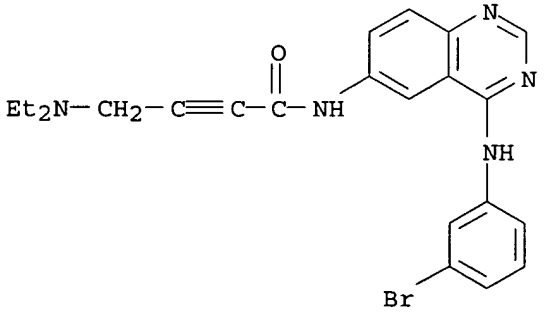
receptor (EGFR) and human epidermal growth factor receptor (HER-2) tyrosine kinases have been prepared These inhibitors have, at the C-6 position, butynamide, crotonamide, and methacrylamide Michael acceptors bearing water-solubilizing substituents. These compds. were prepared by acylation of 6-amino-4-(3-bromophenylamino)quinazoline with unsatd. acid chlorides or mixed anhydrides. We show that attaching a basic functional group onto the Michael acceptor results in greater reactivity, due to intramol. catalysis of the Michael addition and/or an inductive effect of the protonated basic group. This, along with improved water solubility, results in compds. with enhanced biol. properties. We present mol. modeling and exptl. evidence that these inhibitors interact covalently with the target enzymes. One compound, (I) was shown to have excellent oral activity in a human epidermoid carcinoma (A431) xenograft model in nude mice.

IT **220699-39-8P 220699-40-1P 220699-46-7P**
220699-47-8P 220699-48-9P 361392-68-9P
361392-73-6P 361392-74-7P 361392-75-8P
361392-80-5P 361392-81-6P 361392-86-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure activity relations of antitumor (bromophenylamino)quinazolines as putative irreversible inhibitors of EGFR and human epidermal growth factor receptor (HER-2) tyrosine kinase)

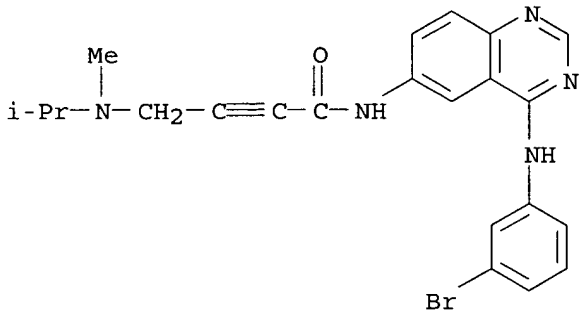
RN 220699-39-8 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



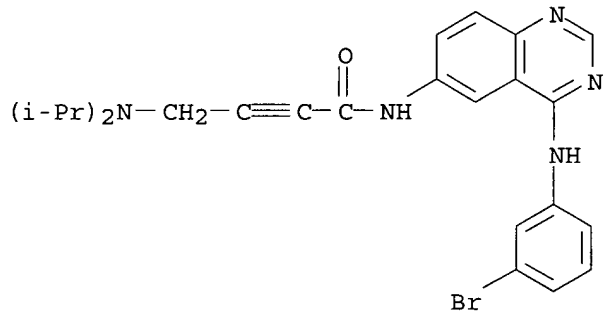
RN 220699-40-1 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



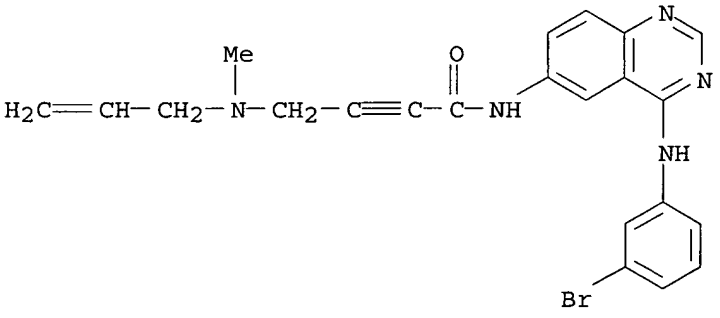
RN 220699-46-7 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



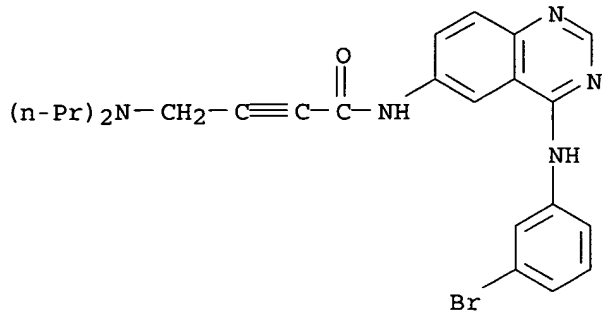
RN 220699-47-8 HCAPLUS
CN 2-Butynamide, 4-[bis(1-methylethyl)amino]-N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 220699-48-9 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(methyl-2-propenylamino)- (9CI) (CA INDEX NAME)

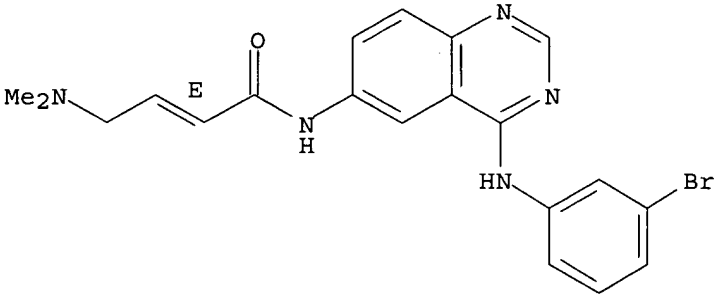


RN 361392-68-9 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dipropylamino)- (9CI) (CA INDEX NAME)



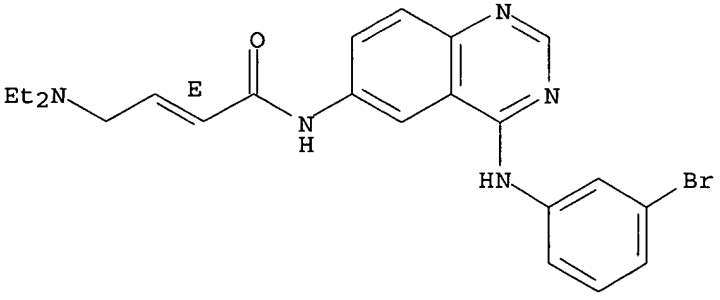
RN 361392-73-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



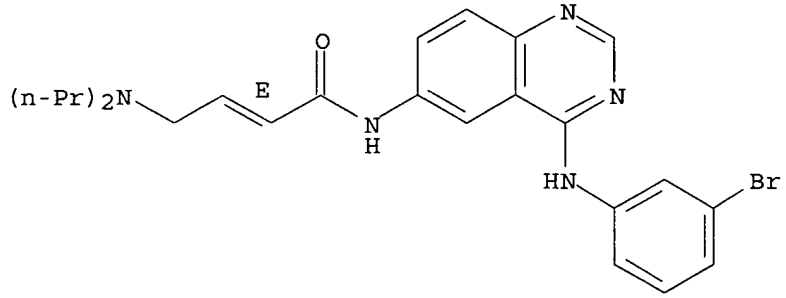
RN 361392-74-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(diethylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



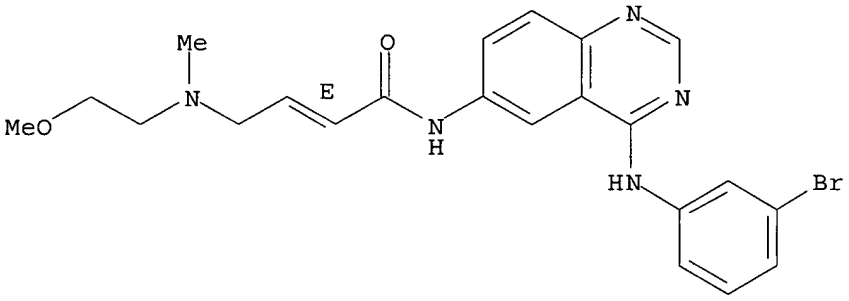
RN 361392-75-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dipropylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



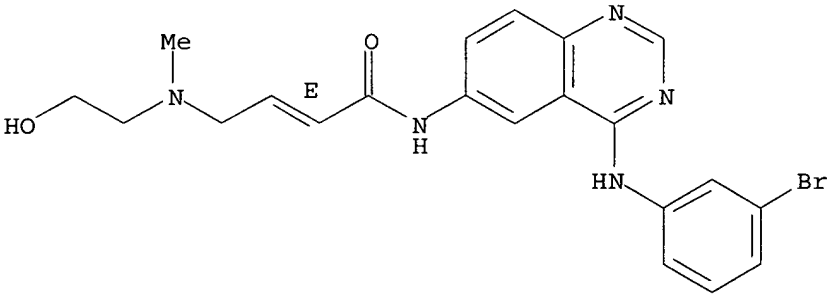
RN 361392-80-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



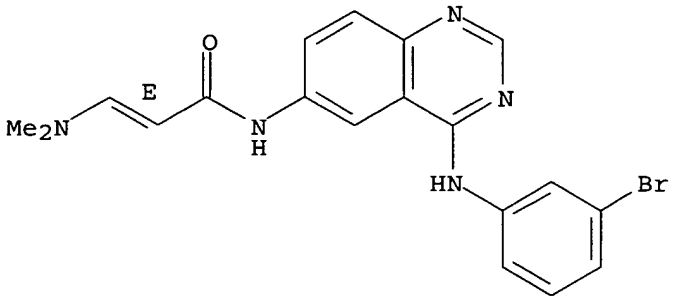
RN 361392-81-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2-hydroxyethyl)methylamino]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 361392-86-1 HCAPLUS
CN 2-Propenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-3-(dimethylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:185 HCAPLUS
DOCUMENT NUMBER: 134:207783
TITLE: Tyrosine kinase inhibitors. 18. 6-Substituted 4-anilinoquinazolines and 4-anilinopyrido[3,4-d]pyrimidines as soluble, irreversible inhibitors of the epidermal growth factor receptor
AUTHOR(S): Smaill, Jeff B.; Showalter, H. D. Hollis; Zhou, Hairong; Bridges, Alexander J.; McNamara, Dennis J.; Fry, David W.; Nelson, James M.; Sherwood, Veronika; Vincent, Patrick W.; Roberts, Bill J.; Elliott, William L.; Denny, William A.
CORPORATE SOURCE: Auckland Cancer Society Research Centre Faculty of Medicine and Health Science, The University of Auckland, Auckland, 92019, N. Z.
SOURCE: Journal of Medicinal Chemistry (2001), 44(3), 429-440
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 4-Anilinoquinazoline- and 4-anilinopyrido[3,4-d]pyrimidine-6-acrylamides are potent pan-erbB tyrosine kinase inactivators, and one example (CI-1033) is in clin. trial. A series of analogs with a variety of Michael acceptor units at the 6-position, I [X = N, C, R1 = H, Me, (CH2)2NMe2, etc., R2 = H, Me, R3 = H, cis-Cl, CF3, etc.], II, and III (X = N, C, R1 = NHSO2CH:CH2, SO2CH2CH2OH, SO2CH:CH2, SOCH:CH2), were prepared to define the structural requirements for irreversible inhibition. A particular goal was to determine whether addnl. functions to increase solubility could be appended to the Michael acceptor. Substituted acrylamides were prepared by direct acylation of the corresponding 6-amines with the requisite acid or acid chloride. Vinylsulfonamide derivs. were obtained by acylation of the amines with chloroethylsulfonyl chloride followed by base-promoted elimination. Vinylsulfone and vinylsulfine derivs. were prepared by oxidation and base elimination of a hydroxyethylthio intermediate. The compds. were evaluated for their inhibition of phosphorylation of the

isolated EGFR enzyme and for inhibition of EGF-stimulated autophosphorylation of EGFR in A431 cells and of heregulin-stimulated autophosphorylation of erbB2 in MDA-MB 453 cells. Substitution at the nitrogen of the acrylamide was tolerated only with a Me group; larger substituents were dystherapeutic, and no substitution at all was tolerated at the acrylamide α-carbon. In contrast, while electron-donating groups at the acrylamide β-carbon were not useful, even quite large electron-withdrawing groups (which increase its electrophilicity) were tolerated. A series of derivs. with solubility-enhancing substituents linked to the acrylamide β-carbon via amides were potent irreversible inhibitors of isolated EGFR (IC50s = 0.4-1.1 nM), with weakly basic morpholine and imidazole derivs. being the best. Vinylsulfonamides were also potent and irreversible inhibitors, but vinylsulfones and vinylsulfines were reversible and only poorly active. Two compds. were evaluated against A431, H125, and MCF-7 xenografts in nude mice but were inferior in these assays to the clin. trial compound CI-1033.

IT **198960-34-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation, epidermal growth factor receptor inhibitory activity, and structure-activity relationship of anilinoquinazolines and -pyridopyrimidines)

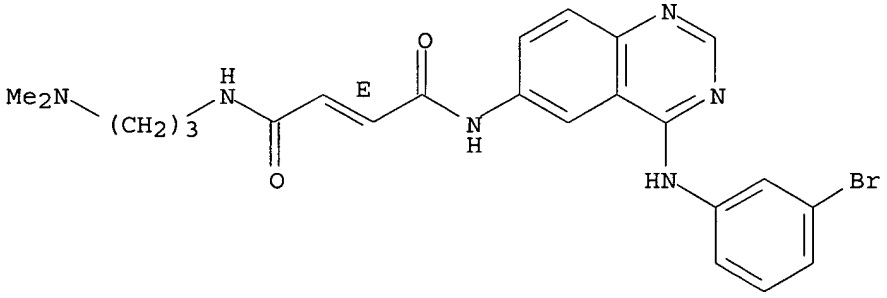
RN 198960-34-8 HCAPLUS

CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]-, (2E)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

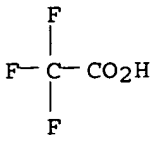
CRN 198960-33-7
CMF C23 H25 Br N6 O2

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:911231 HCAPLUS
DOCUMENT NUMBER: 134:71599
TITLE: Preparation of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors.
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Metz, Thomas; Solca, Flavio; Jung, Birgit; Baum, Anke
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078735	A1	20001228	WO 2000-EP5547	20000616
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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DE 10023085	A1	20011115	DE 2000-10023085	20000511
CA 2375259	AA	20001228	CA 2000-2375259	20000616
BR 2000011834	A	20020312	BR 2000-11834	20000616
EP 1194418	A1	20020410	EP 2000-936888	20000616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103692	T2	20021021	TR 2001-200103692	20000616
JP 2003502410	T2	20030121	JP 2001-504901	20000616
JP 3686610	B2	20050824		
EE 200100695	A	20030217	EE 2001-695	20000616
AU 775285	B2	20040729	AU 2000-52214	20000616
NZ 516633	A	20040924	NZ 2000-516633	20000616
BG 106189	A	20020830	BG 2001-106189	20011207
US 2002169180	A1	20021114	US 2001-16280	20011210
NO 2001006185	A	20011218	NO 2001-6185	20011218
ZA 2001010351	A	20020618	ZA 2001-10351	20011218
HK 1044769	A1	20050225	HK 2002-106291	20020827

PRIORITY APPLN. INFO.:	DE 1999-19928281	A	19990621
	US 1999-146644P	P	19990730
	DE 2000-10023085	A	20000511

WO 2000-EP5547 W 20000616

OTHER SOURCE(S): MARPAT 134:71599

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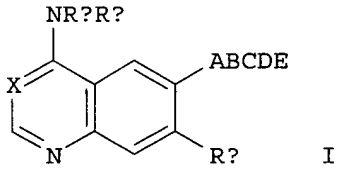


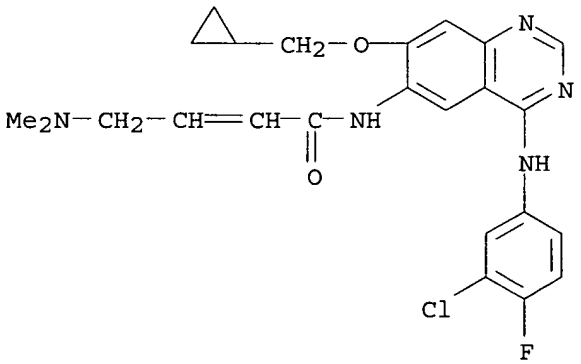
I

AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH2, PhCH2CH2; Rc = (substituted) cycloalkoxy, cycloalkylalkoxy; A = (alkyl-substituted) imino; B = CO, SO2; C = (substituted) allenylene, vinylene, butadienylene, ethynylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, carbonyloxyalkylene, carbonyliminoalkylene, bond, etc.; E = amino, (substituted) alkylamino, dialkylamino, etc.], were prepared Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propoxy]quinazoline (preparation given) in CH2Cl2 containing Et3N at -10° was treated with acryloyl chloride in THF to give 35% 4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation of F/L HERC cells with IC50 = <0.35 nM.

IT **314771-10-3P 314771-37-4P 314771-38-5P**
314771-42-1P 314771-43-2P 314771-44-3P
314771-45-4P 314771-48-7P 314771-49-8P
314771-55-6P 314771-58-9P 314771-59-0P
314771-61-4P 314771-62-5P 314771-63-6P
314771-66-9P 314771-67-0P 314771-68-1P
314771-69-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors)

RN 314771-10-3 HCAPLUS

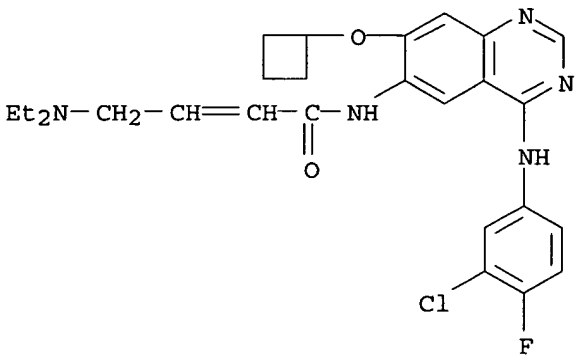
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



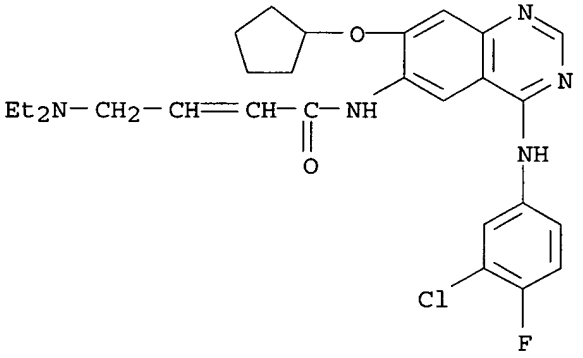
RN 314771-37-4 HCAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-

quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

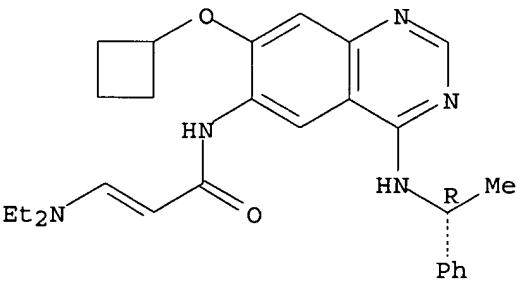


RN 314771-38-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



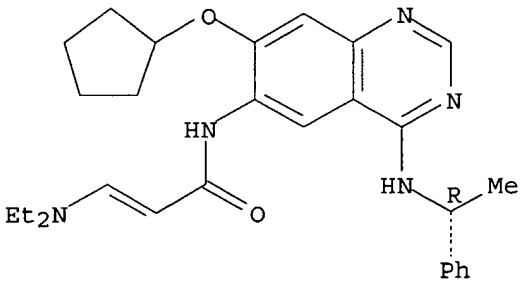
RN 314771-42-1 HCAPLUS
CN 2-Propenamide, N-[7-(cyclobutyloxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-3-(diethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



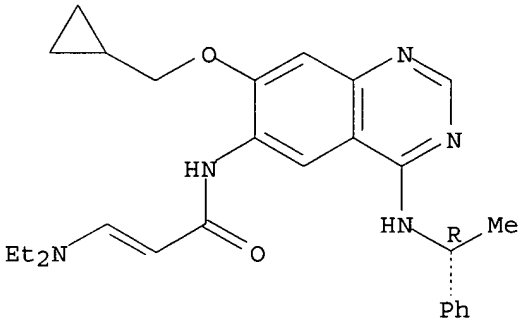
RN 314771-43-2 HCAPLUS
CN 2-Propenamide, N-[7-(cyclopentyloxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-3-(diethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

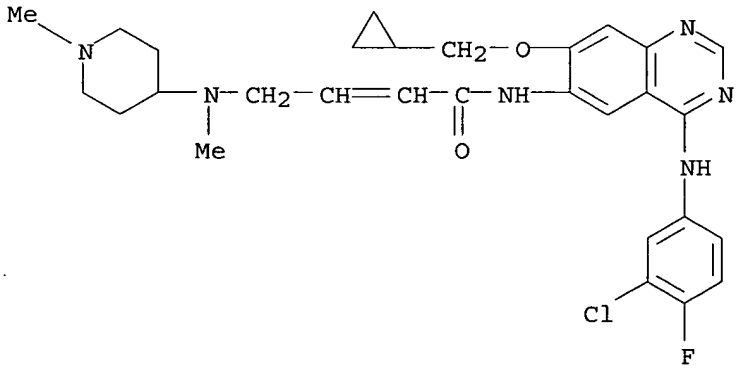


RN 314771-44-3 HCAPLUS
CN 2-Propenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-3-(diethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

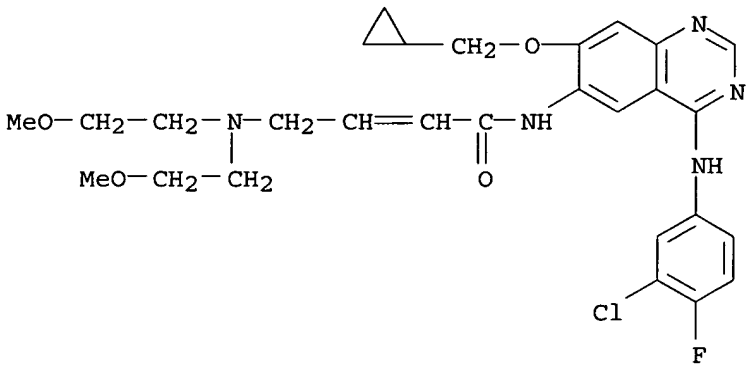


RN 314771-45-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(1-methyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)

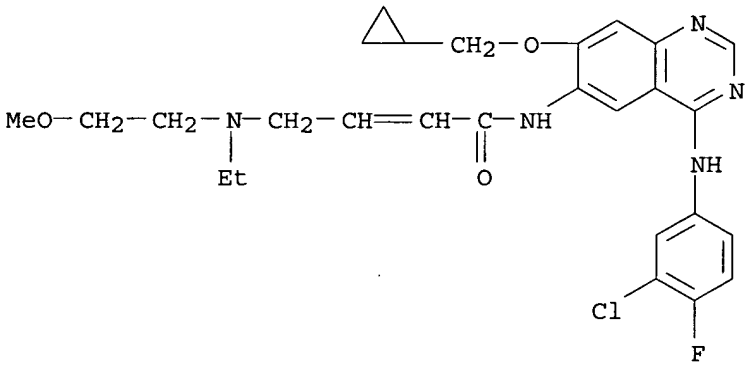


RN 314771-48-7 HCAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-

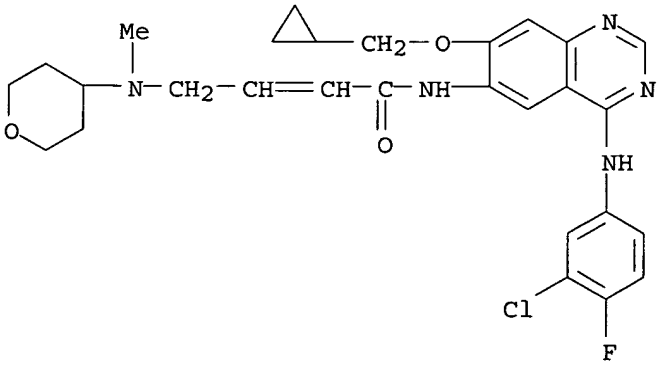
fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



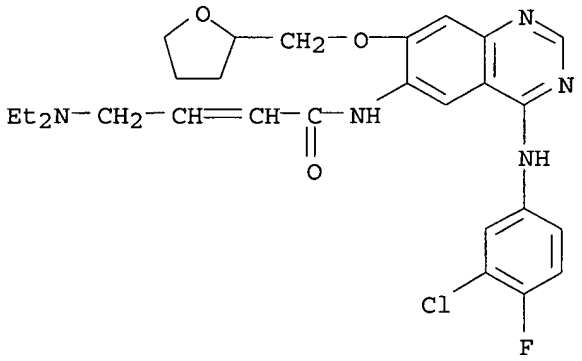
RN 314771-49-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)



RN 314771-55-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

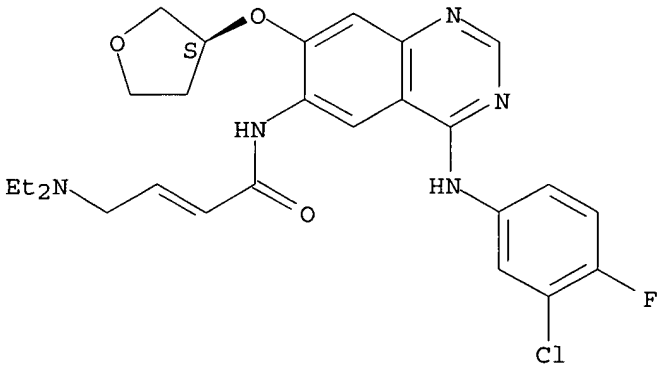


RN 314771-58-9 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

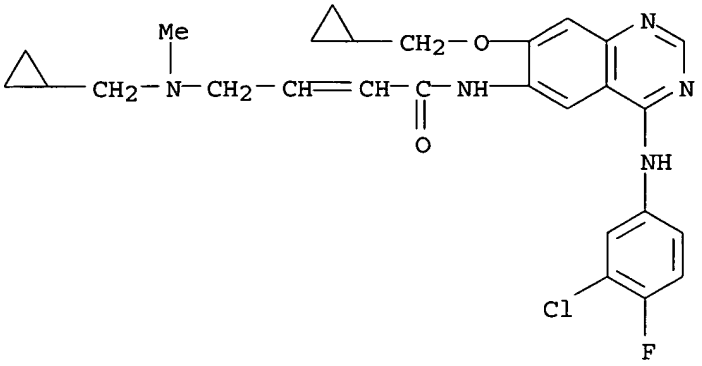


RN 314771-59-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

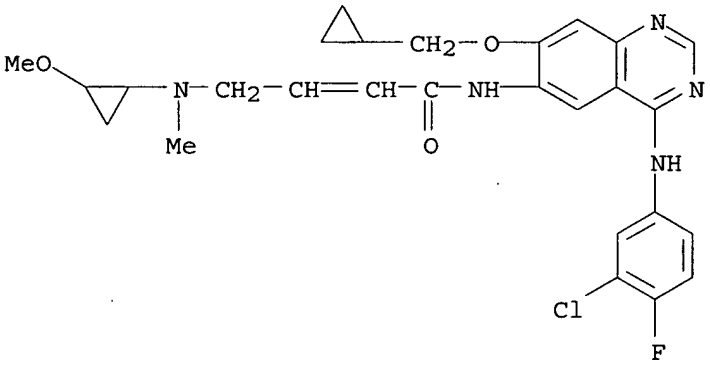
Absolute stereochemistry.
Double bond geometry unknown.



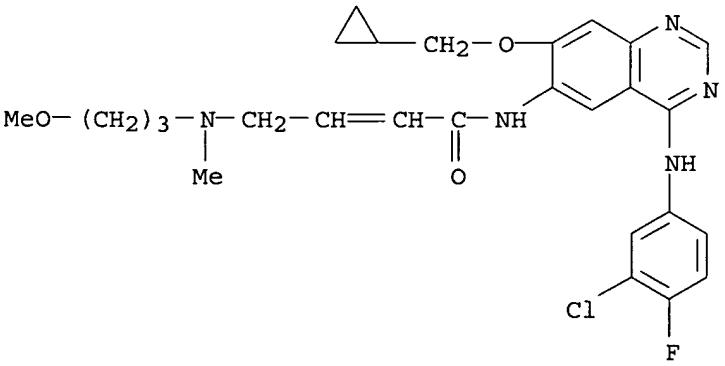
RN 314771-61-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(cyclopropylmethyl)methylamino]- (9CI) (CA INDEX NAME)



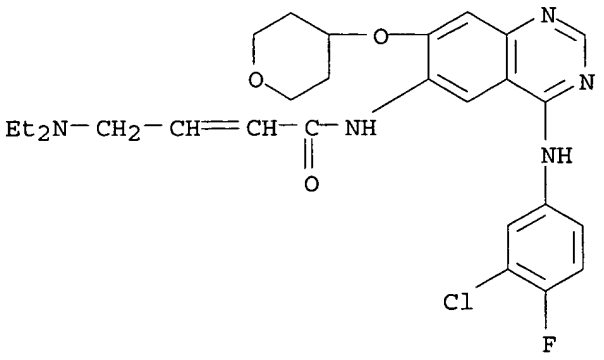
RN 314771-62-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxycyclopropyl)methylamino]- (9CI) (CA INDEX NAME)



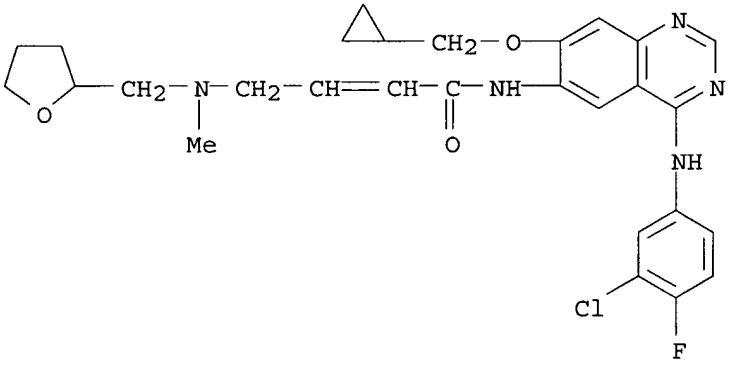
RN 314771-63-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3-methoxypropyl)methylamino]- (9CI) (CA INDEX NAME)



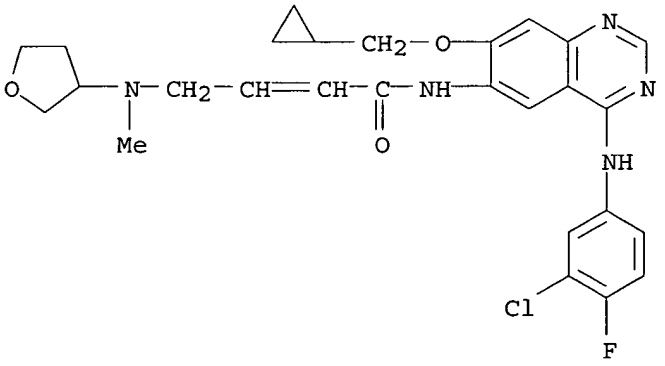
RN 314771-66-9 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



RN 314771-67-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

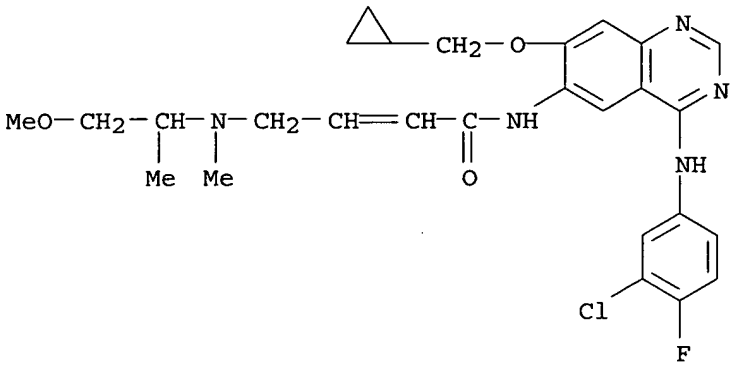


RN 314771-68-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-3-furanyl)amino]- (9CI) (CA INDEX NAME)



RN 314771-69-2 HCAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxy-1-methylethyl)methylamino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:628125 HCAPLUS
DOCUMENT NUMBER: 133:207919
TITLE: Preparation of 4-amino-quinazoline and quinoline derivatives having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas; Solca, Flavio; Blech, Stefan
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051991	A1	20000908	WO 2000-EP1496	20000224
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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DE 19911366	A1	20000921	DE 1999-19911366	19990315
DE 19928306	A1	20001228	DE 1999-19928306	19990621
DE 19954816	A1	20010517	DE 1999-19954816	19991113
CA 2361174	AA	20000908	CA 2000-2361174	20000224
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IE, SI, LT, LV, FI, RO					
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BG 105765	A	20020329	BG 2001-105765		20010801
HR 2001000617	A1	20021031	HR 2001-617		20010823
NO 2001004114	A	20011015	NO 2001-4114		20010824
PRIORITY APPLN. INFO.:			DE 1999-19908567	A	19990227
			DE 1999-19911366	A	19990315
			DE 1999-19928306	A	19990621
			US 1999-149329P	P	19990817
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			WO 2000-EP1496	W	20000224

OTHER SOURCE(S): MARPAT 133:207919

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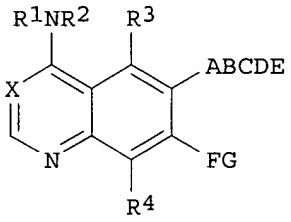

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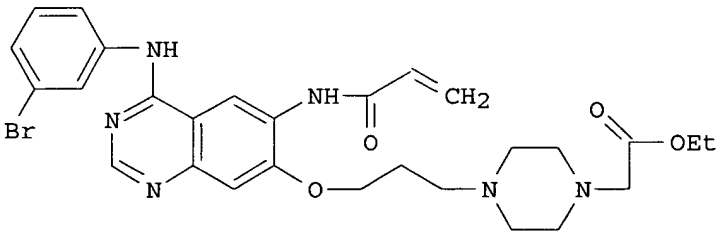


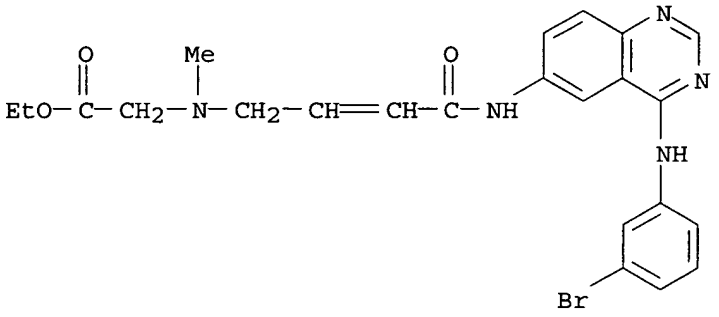
II

AB Title compds. [I; R1 = H, C1-C4-alkyl; R2 = (un)substituted Ph, benzyl, 1-phenylethyl; R3, R4 independently = H, F, Cl, CH3O, CH3OCH2, (CH3)2NCH2, (CH3CH2)2NCH2, pyrrolidino, piperidino, morpholino; X = C(CN), N; A = O, NH, (C1-C4)-alkylN; B = CO, SO2; C = 1,3-allenylene, 1,1-vinylene, 1,2-vinylene, 1,3-butadien-1,4-ylene, with CH3, CF3 substitution; D = alkylene, CO-alkylene, SO2-alkylene; CO, SO2; E = HOCO(CH2)nNR5, (HO)2P(:O)(CH2)nNR5; n = 1-6; R5 = H, alkyl], tautomers, stereoisomers, and physiol. acceptable salts are prepared and having valuable pharmacol. properties, particularly an inhibiting effect on signal transduction mediated by tyrosine kinases. Title compds. are useful for treating tumoral diseases, diseases of the lungs and respiratory tract. Thus, the title compound II was prepared and tested by Cell Titer 96TM Aqueous Nonradioactive Cell Proliferation Assay.

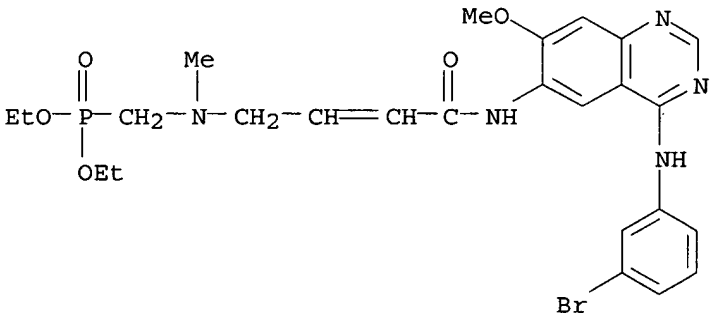
IT **289700-68-1P 290301-75-6P 290301-88-1P 290301-94-9P 290302-19-1P 290302-98-6P**

290303-04-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 289700-68-1 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

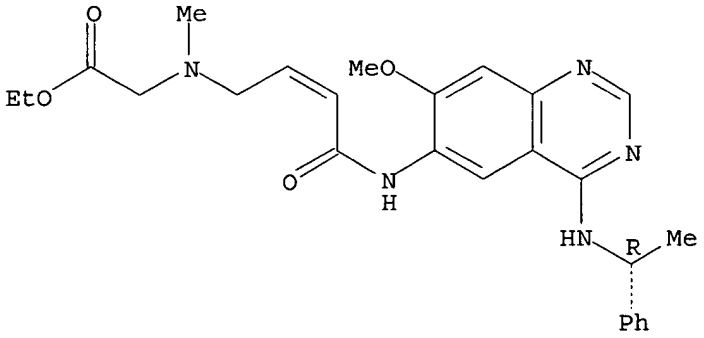


RN 290301-75-6 HCAPLUS
CN Phosphonic acid, [[[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]methyl]-, diethyl ester (9CI) (CA INDEX NAME)

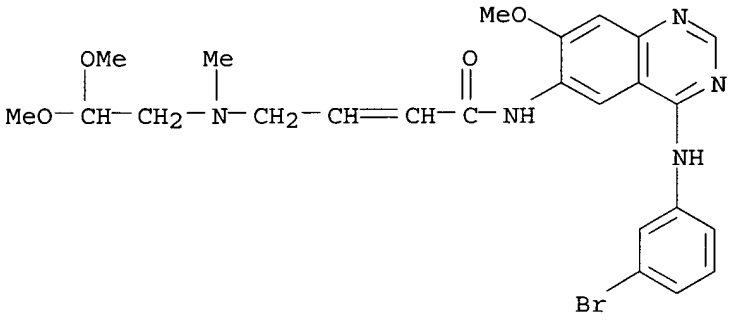


RN 290301-88-1 HCAPLUS
CN Glycine, N-[4-[[7-methoxy-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

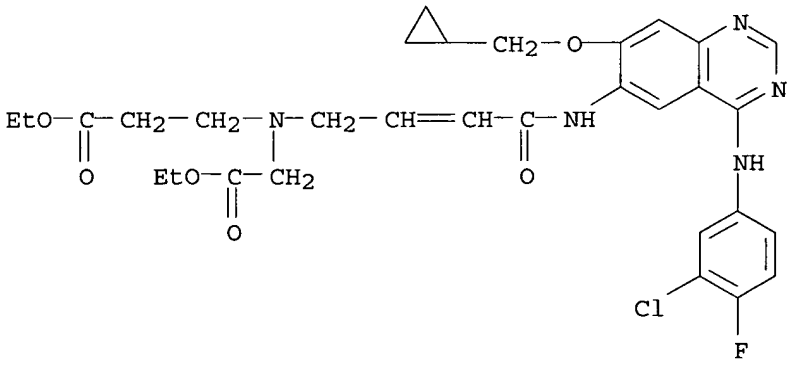
Absolute stereochemistry.
Double bond geometry unknown.



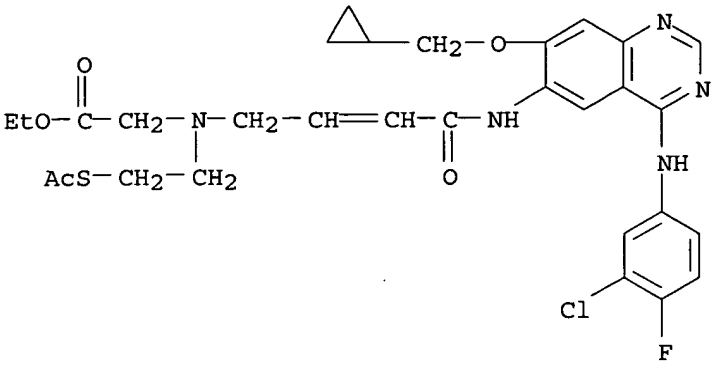
RN 290301-94-9 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(2,2-dimethoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



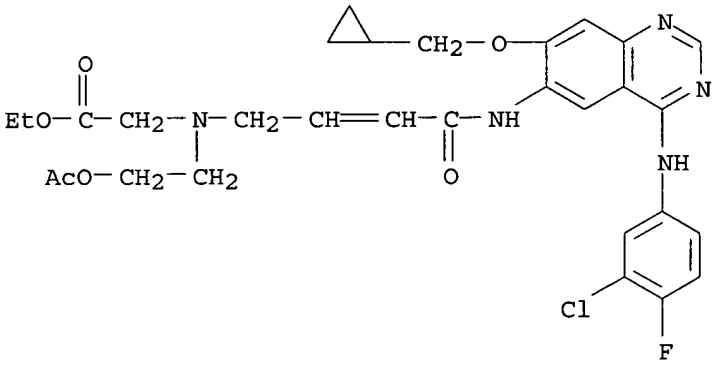
RN 290302-19-1 HCAPLUS
CN β-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



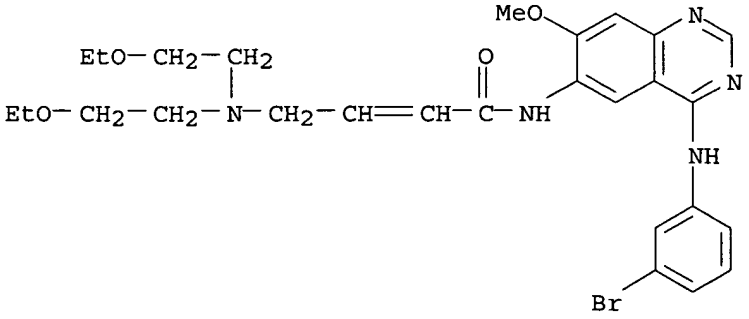
RN 290302-98-6 HCAPLUS
CN Glycine, N-[2-(acetylthio)ethyl]-N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



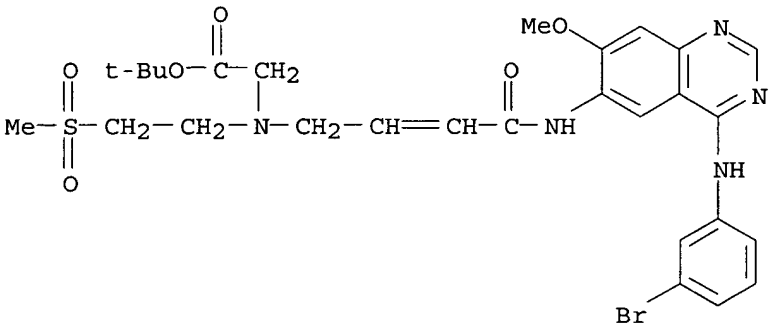
RN 290303-04-7 HCAPLUS
CN Glycine, N-[2-(acetyloxy)ethyl]-N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT **290304-09-5 290304-10-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)
RN 290304-09-5 HCAPLUS
CN 2-Butenamide, 4-[bis(2-ethoxyethyl)amino]-N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]- (9CI) (CA INDEX NAME)

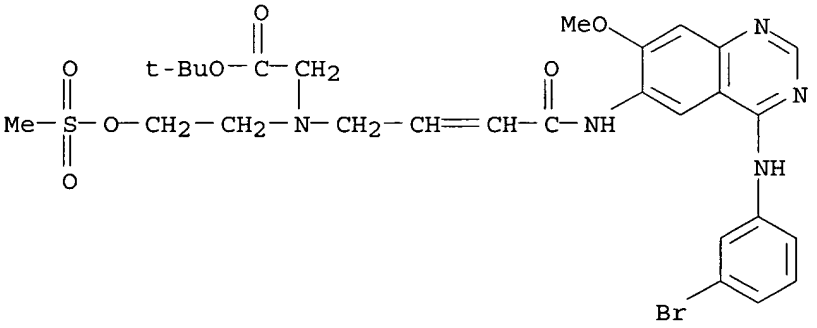


RN 290304-10-8 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-(methylsulfonyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

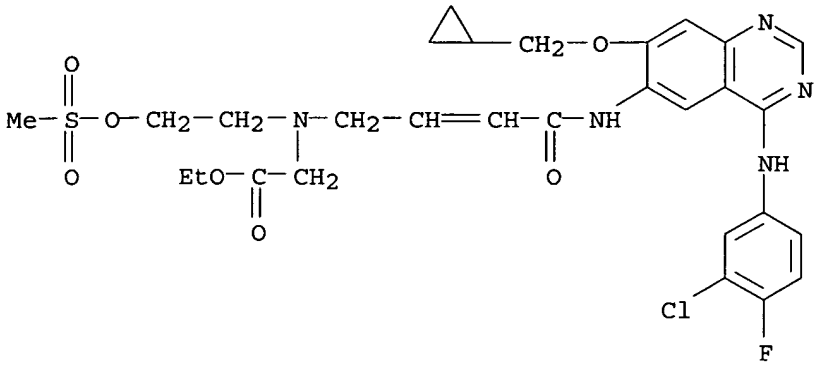


IT **290303-83-2P 290303-84-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 290303-83-2 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-[(methylsulfonyl)oxy]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



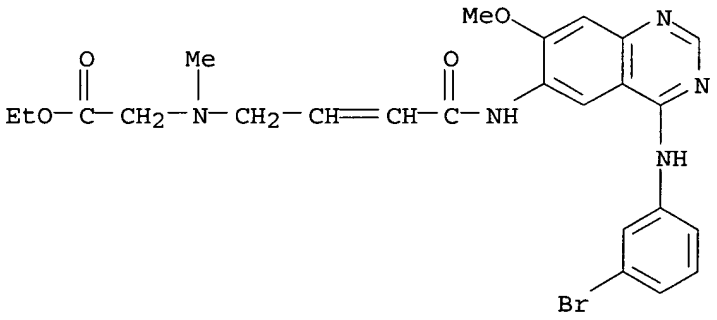
RN 290303-84-3 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-[(methylsulfonyl)oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT **289700-69-2P 290301-73-4P 290301-77-8P**
290301-78-9P 290301-79-0P 290301-80-3P
290301-86-9P 290301-87-0P 290301-89-2P
290301-90-5P 290301-91-6P 290301-95-0P
290302-01-1P 290302-07-7P 290302-09-9P
290302-15-7P 290302-23-7P 290302-27-1P
290302-43-1P 290302-49-7P 290302-71-5P
290302-83-9P 290302-89-5P 290302-93-1P
290302-94-2P 290302-97-5P 290302-99-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

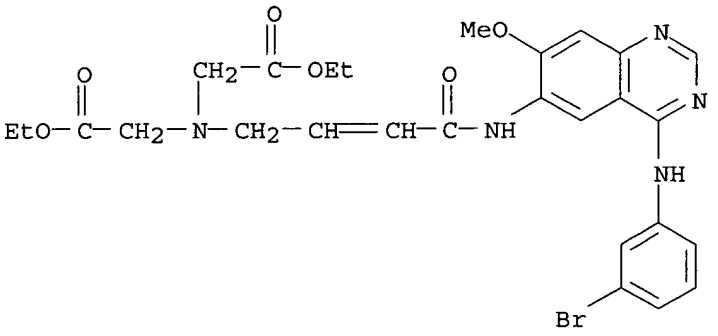
RN 289700-69-2 HCAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

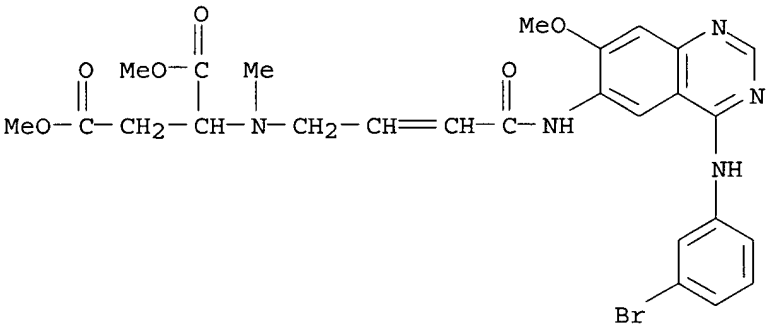


RN 290301-73-4 HCAPLUS

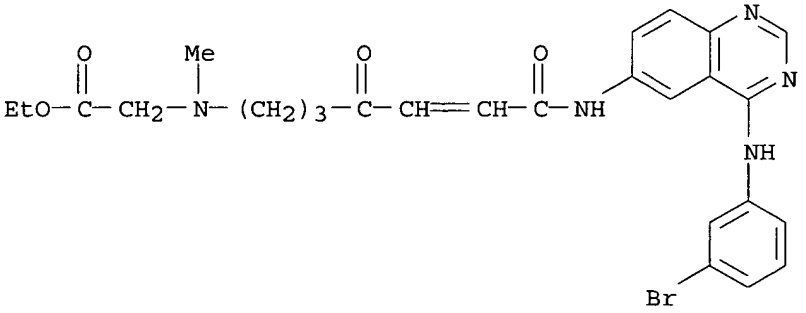
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



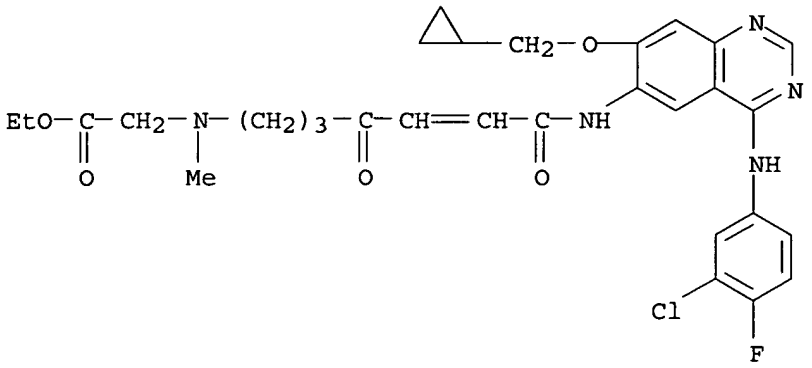
RN 290301-77-8 HCAPLUS
CN Aspartic acid, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, dimethyl ester (9CI) (CA INDEX NAME)



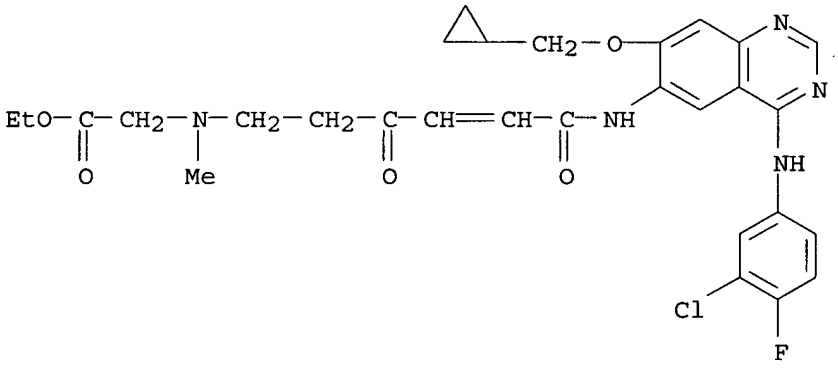
RN 290301-78-9 HCAPLUS
CN Glycine, N-[7-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4,7-dioxo-5-heptenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



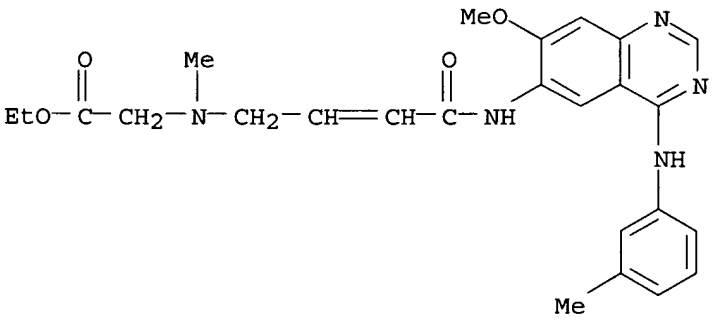
RN 290301-79-0 HCAPLUS
CN Glycine, N-[7-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4,7-dioxo-5-heptenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



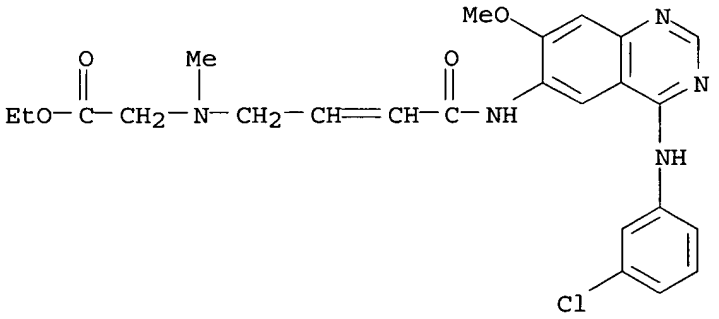
RN 290301-80-3 HCAPLUS
CN Glycine, N-[6-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-3,6-dioxo-4-hexenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



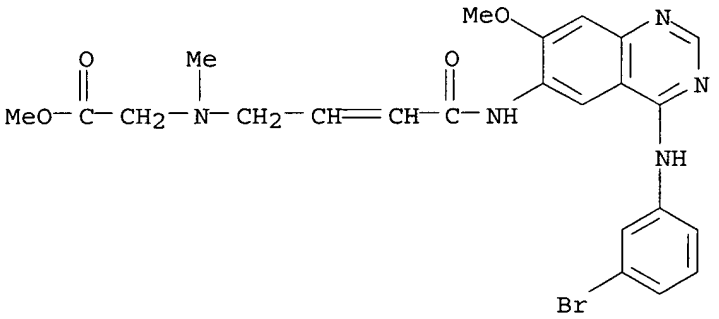
RN 290301-86-9 HCAPLUS
CN Glycine, N-[4-[[7-methoxy-4-[(3-methylphenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



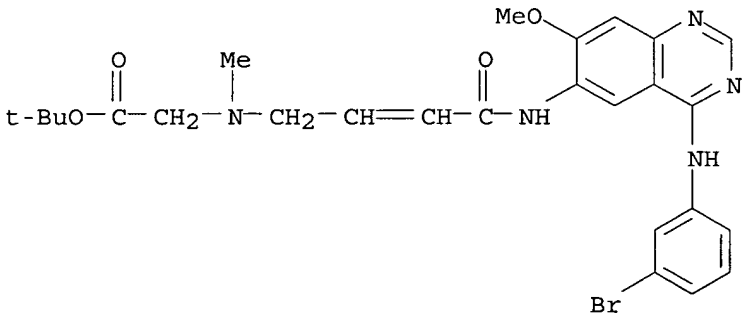
RN 290301-87-0 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chlorophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



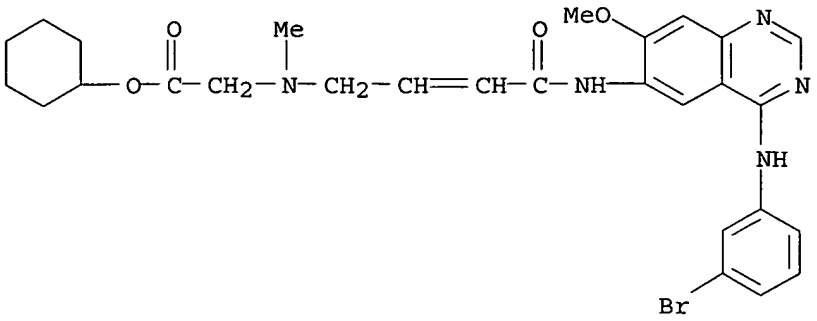
RN 290301-89-2 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)



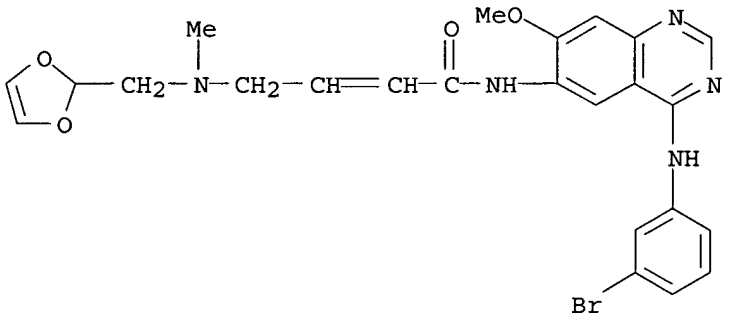
RN 290301-90-5 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



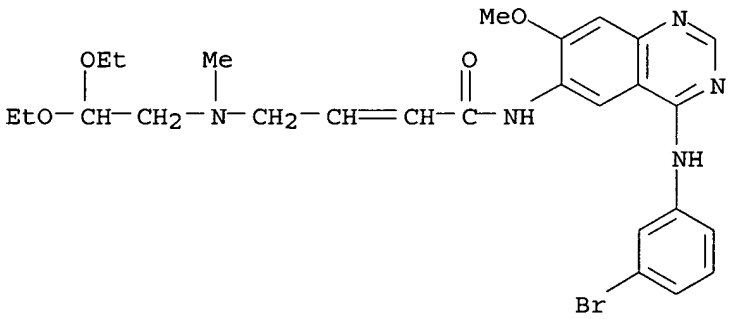
RN 290301-91-6 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, cyclohexyl ester (9CI) (CA INDEX NAME)



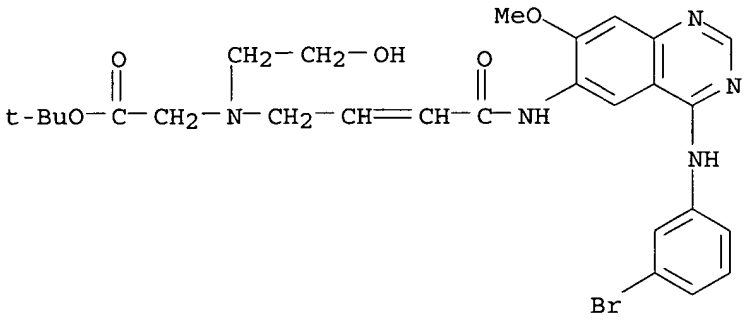
RN 290301-95-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(1,3-dioxol-2-ylmethyl)methylamino]- (9CI) (CA INDEX NAME)



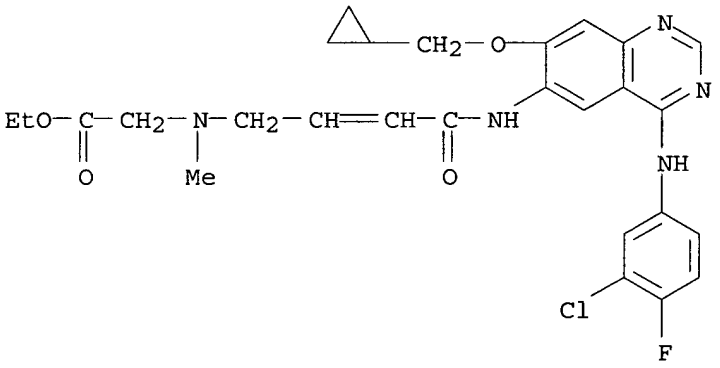
RN 290302-01-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(2,2-diethoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



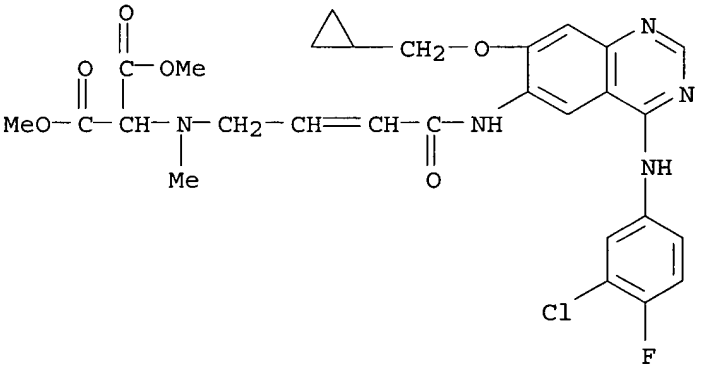
RN 290302-07-7 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



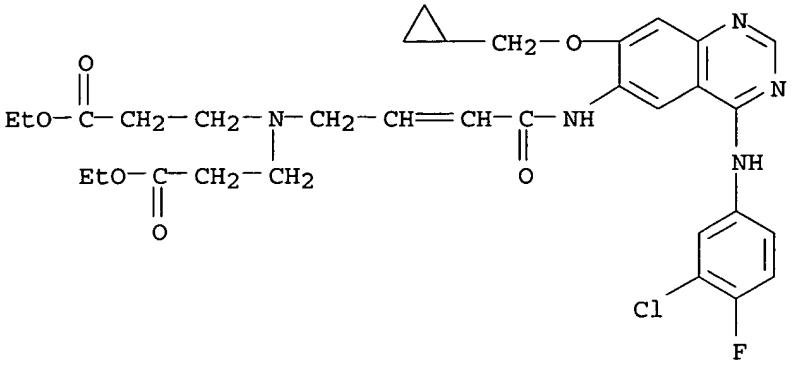
RN 290302-09-9 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



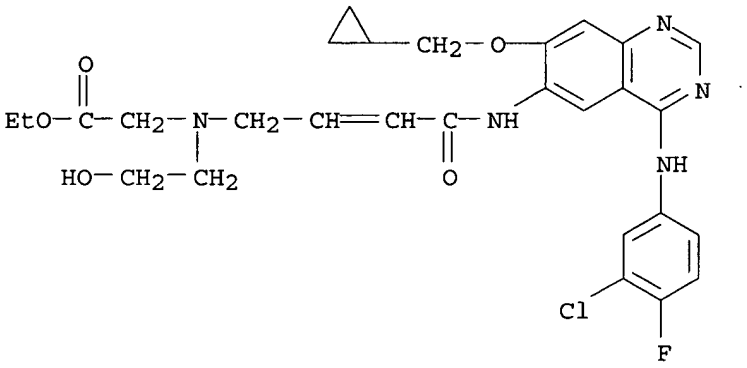
RN 290302-15-7 HCAPLUS
CN Propanedioic acid, [[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]-, dimethyl ester (9CI) (CA INDEX NAME)



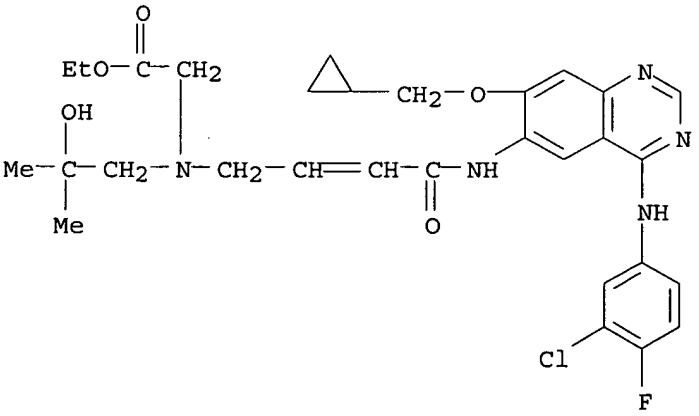
RN 290302-23-7 HCAPLUS
CN β-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(3-ethoxy-3-oxopropyl)-, ethyl ester (9CI) (CA INDEX NAME)



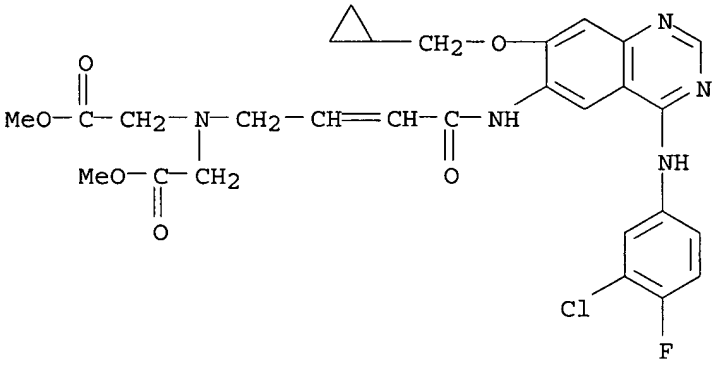
RN 290302-27-1 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)



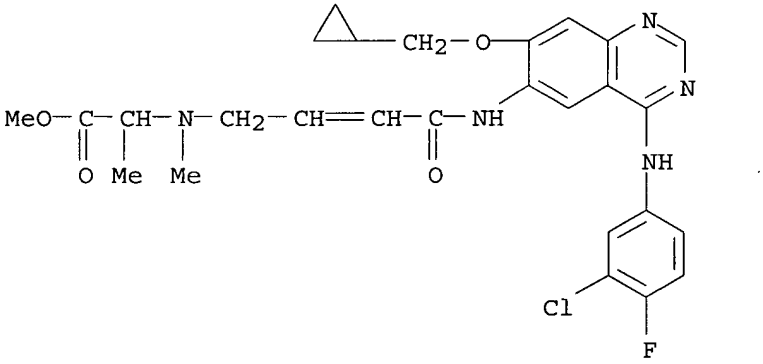
RN 290302-43-1 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)-, ethyl ester (9CI) (CA INDEX NAME)



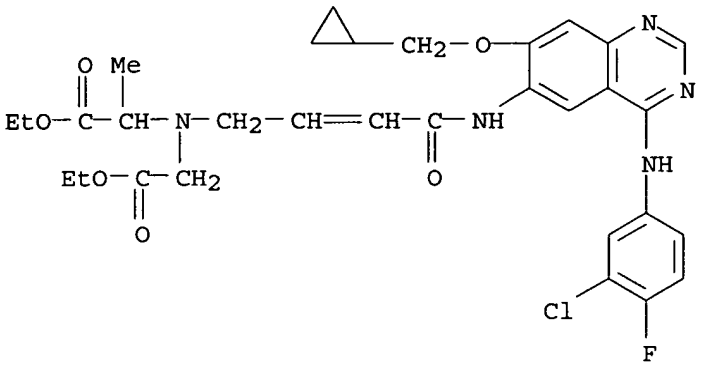
RN 290302-49-7 HCAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-methoxy-2-oxoethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 290302-71-5 HCAPLUS
CN Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)

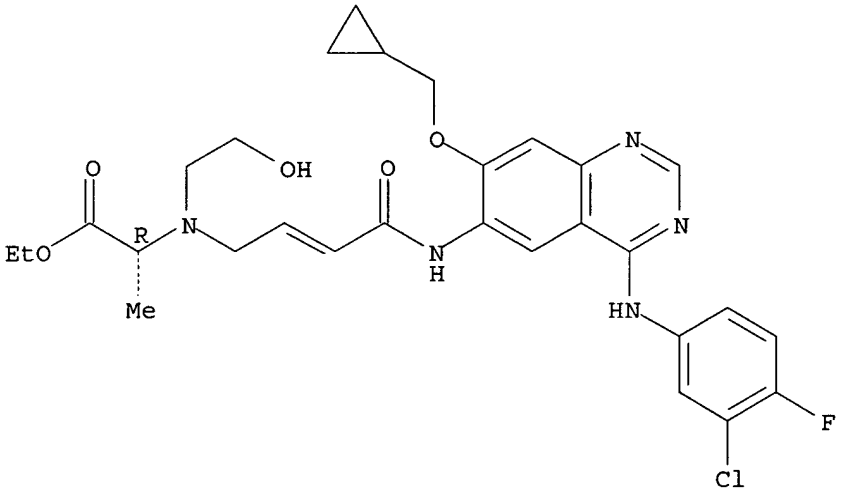


RN 290302-83-9 HCAPLUS
CN Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

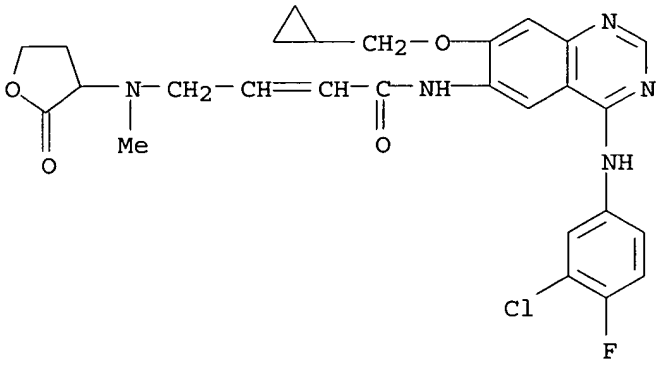


RN 290302-89-5 HCAPLUS
CN D-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

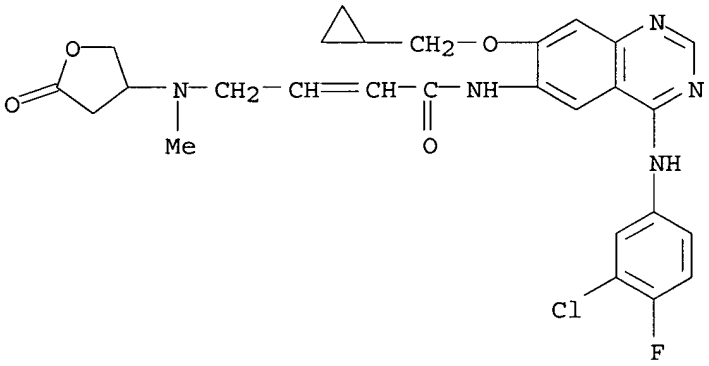
Absolute stereochemistry.
Double bond geometry unknown.



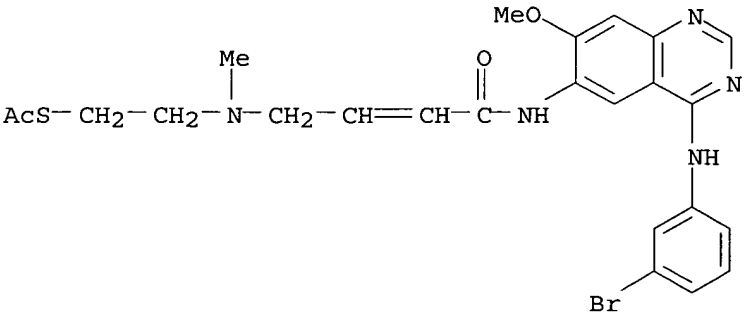
RN 290302-93-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]- (9CI) (CA INDEX NAME)



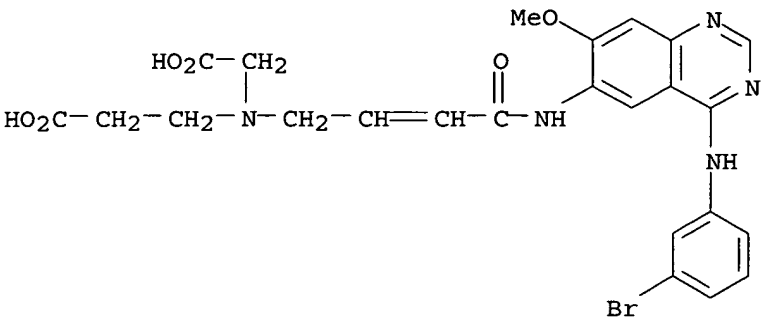
RN 290302-94-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-5-oxo-3-furanyl)amino]- (9CI) (CA INDEX NAME)



RN 290302-97-5 HCAPLUS
CN Ethanethioic acid, S-[2-[[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]ethyl] ester (9CI) (CA INDEX NAME)



RN 290302-99-7 HCAPLUS
CN β-Alanine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(carboxymethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

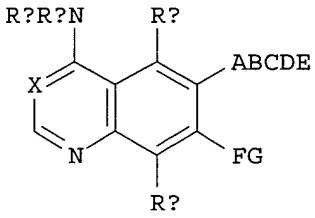
L8 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:607393 HCAPLUS
DOCUMENT NUMBER: 133:207916
TITLE: Preparation of aminoquinazolines as epidermal growth factor receptor inhibitors.
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K-G, Germany
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908567	A1	20000831	DE 1999-19908567	19990227
CA 2361174	AA	20000908	CA 2000-2361174	20000224
WO 2000051991	A1	20000908	WO 2000-EP1496	20000224
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 513802	A	20010928	NZ 2000-513802	20000224
EP 1157011	A1	20011128	EP 2000-910695	20000224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008524	A	20011218	BR 2000-8524	20000224
JP 2002538145	T2	20021112	JP 2000-602218	20000224
EE 200100449	A	20021216	EE 2001-449	20000224
ZA 2001005983	A	20020920	ZA 2001-5983	20010720
BG 105765	A	20020329	BG 2001-105765	20010801
HR 2001000617	A1	20021031	HR 2001-617	20010823
NO 2001004114	A	20011015	NO 2001-4114	20010824

PRIORITY APPLN. INFO.: DE 1999-19908567 A 19990227
DE 1999-19911366 A 19990315

	DE 1999-19928306	A	19990621
	US 1999-149329P	P	19990817
	DE 1999-19954816	A	19991113
	WO 2000-EP1496	W	20000224

OTHER SOURCE(S): MARPAT 133:207916
GI

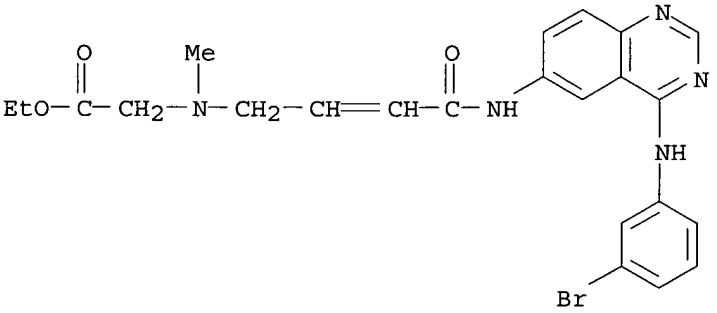


I

AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH2, 1-phenylethyl; Rc, Rm = H, F, Cl, MeO, (methoxy-, dimethylamino-, diethylamino-, pyrrolidino-, piperidino-, morpholino- substituted) Me; X = N, NCC; A = O, alkylimino; B = CO, SO2; C = (Me- or F3C-substituted) allenylene, vinylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, etc.; E, G = (substituted) R6O2CYNR5, etc.; R5 = H, (substituted) alkyl; R6 = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl, etc.; F = alkylene, oxyalkylene, O; FG = H, F, Cl, alkoxy, etc.], were prepared Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-[4-(ethoxycarbonyl)methylpiperazin-1-yl]propoxy]quinazoline (preparation given) in CH2Cl2 containing Et3N was treated with acryloyl chloride in CH2Cl2 at -10° to give 62% 4-[(3-bromophenyl)amino]-7-[3-[4-[(ethoxycarbonyl)methyl]piperazin-1-yl]propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation with IC50 = 2.6 nM.

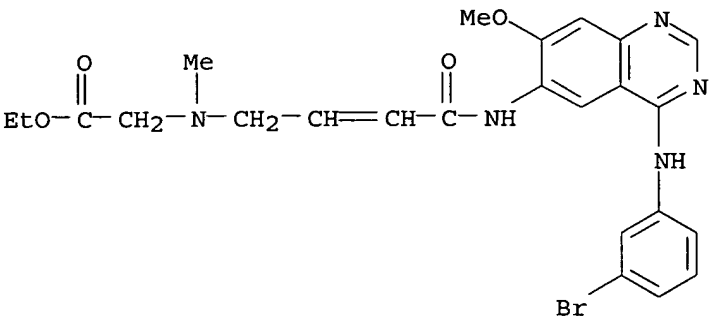
IT **289700-68-1P 289700-69-2P 289700-70-5P 289700-71-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoquinazolines as epidermal growth factor receptor inhibitors)

RN 289700-68-1 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

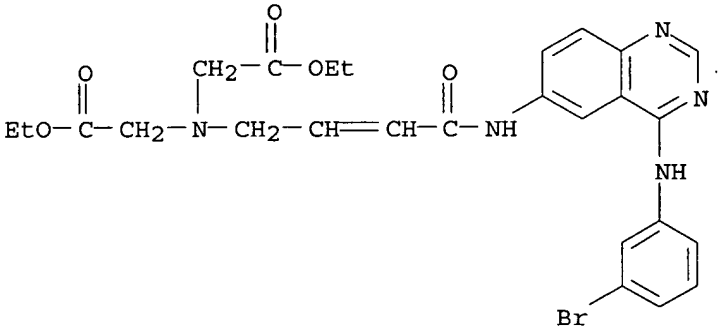


RN 289700-69-2 HCAPLUS

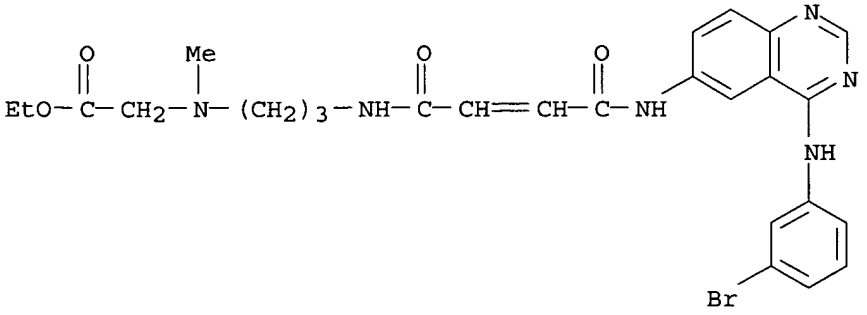
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-70-5 HCAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-71-6 HCAPLUS
CN Glycine, N-[3-[[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]amino]propyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:139833 HCAPLUS
DOCUMENT NUMBER: 130:196664
TITLE: Preparation of 4-phenylaminoquinazolin-6-ylamides and

related compounds as tyrosine kinase inhibitors.

INVENTOR(S): Wissner, Allan; Tsou, Hwei-ru; Johnson, Bernard Dean; Hamann, Philip Ross; Zhang, Nan

PATENT ASSIGNEE(S): American Cyanamid Company, USA

SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

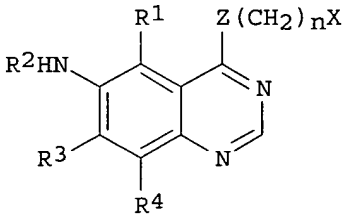
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9909016	A1	19990225	WO 1998-US15789		19980729
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
TW 436485	B	20010528	TW 1998-87112356		19980728
CA 2299632	AA	19990225	CA 1998-2299632		19980729
AU 9886023	A1	19990308	AU 1998-86023		19980729
AU 757418	B2	20030220			
EP 1000039	A1	20000517	EP 1998-937275		19980729
EP 1000039	B1	20040609			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO					
BR 9811805	A	20000815	BR 1998-11805		19980729
US 6251912	B1	20010626	US 1998-124365		19980729
JP 2001515071	T2	20010918	JP 2000-509699		19980729
RU 2227798	C2	20040427	RU 2000-105243		19980729
AT 268761	E	20040615	AT 1998-937275		19980729
PT 1000039	T	20040930	PT 1998-937275		19980729
ES 2222599	T3	20050201	ES 1998-937275		19980729
ZA 9806905	A	20000131	ZA 1998-6905		19980731
NO 2000000487	A	20000331	NO 2000-487		20000131
HK 1026209	A1	20041112	HK 2000-105391		20000829
NZ 519387	A	20040326	NZ 2002-519387		20020606
PRIORITY APPLN. INFO.:			US 1997-904942	A	19970801
			US 1997-55072P	P	19970801
			WO 1998-US15789	W	19980729
			NZ 2002-501885	A1	20020606

OTHER SOURCE(S): MARPAT 130:196664

GI

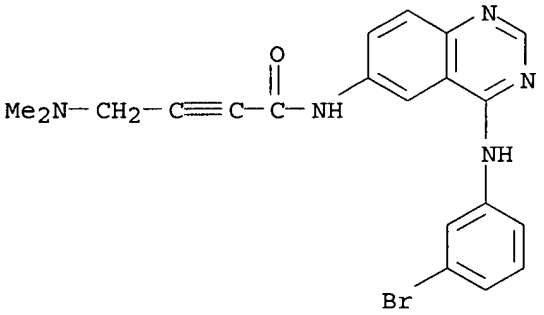


I

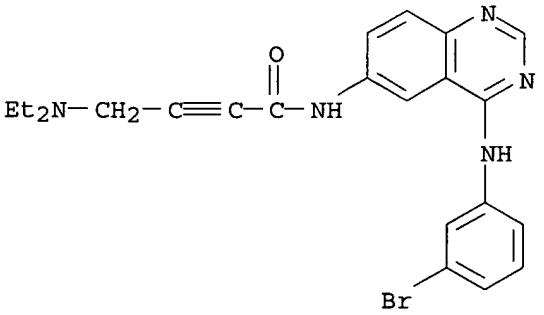
AB Title compds. [I; X = (substituted) cycloalkyl, pyridinyl, pyrimidinyl, Ph; Z = NH, O, S, NR; R = alkyl; R1, R3, R4 = H, halo, alkyl, alkenyl, alkynyl, alkenyloxy, alkynyloxy, CH2OH, halomethyl, alkanoyloxy, alkenoyloxy, alkynoyloxy, alkanoyloxymethyl, etc.; R2 = R5C.tplbond.CCO, (R5)2C:CR5CO, R5SS[C(R5)2]rCO, etc.; n = 0, 1; r = 1-4; R5 = H, CO2H, carboalkoxy, Ph, etc.], were prepared Thus, 4-dimethylamino-2-butynoic acid (preparation given) was stirred with iso-Bu chloroformate and N-methylmorpholine in THF with ice cooling; N-(3-bromophenyl)-4,6-quinazolinediamine in pyridine was added and the mixture was stirred 2 h at 0° to give 4-dimethylamino-2-butynoic acid [4-(3-bromophenylamino)quinazolin-6-yl]amide. The latter inhibited MB435 tumor cell growth with IC50 = 0.05 μg/mL.

IT **220699-39-8P 220699-40-1P 220699-43-4P**
220699-45-6P 220699-46-7P 220699-47-8P
220699-48-9P 220699-51-4P 220699-67-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-phenylaminoquinazolin-6-ylamides and related compds. as tyrosine kinase inhibitors)

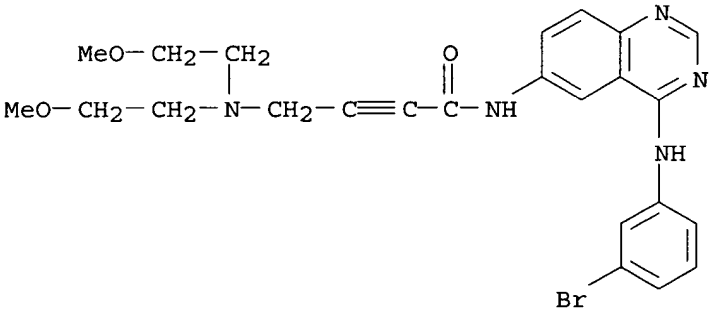
RN 220699-39-8 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



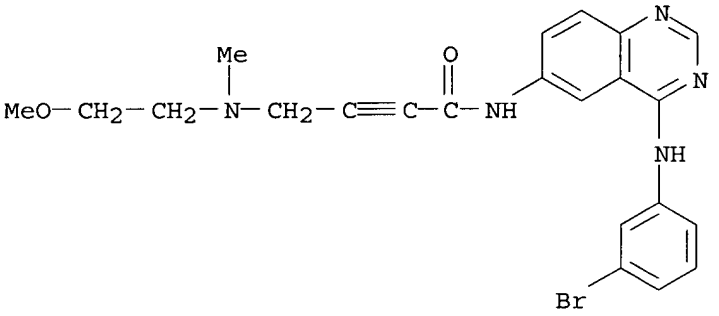
RN 220699-40-1 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



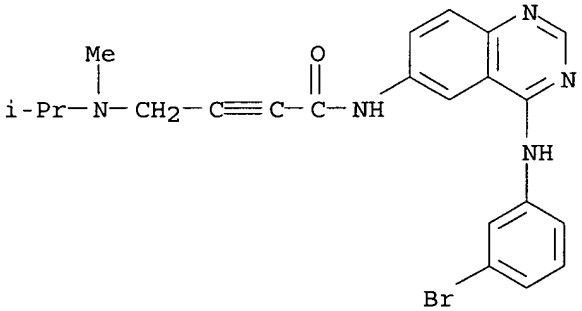
RN 220699-43-4 HCAPLUS
CN 2-Butynamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 220699-45-6 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



RN 220699-46-7 HCAPLUS
CN 2-Butynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



RN 220699-47-8 HCAPLUS
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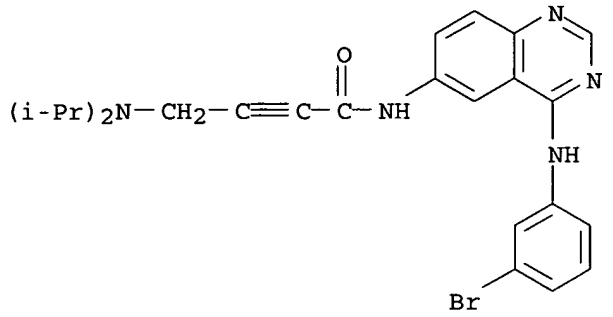

RN 220699-48-9 HCAPLUS
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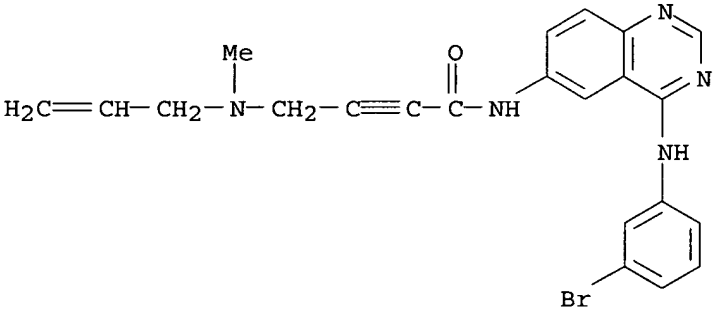
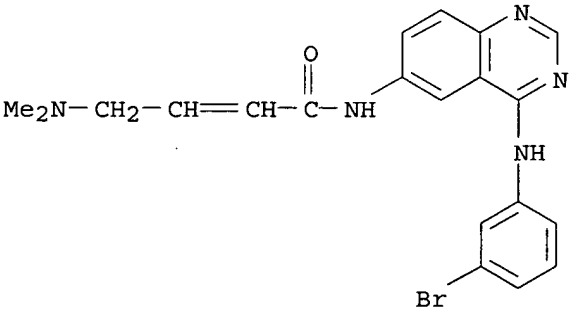
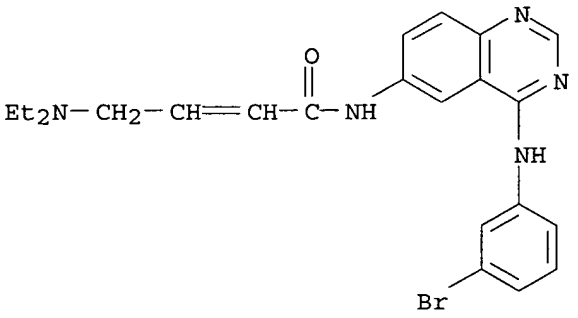


RN 220699-51-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 220699-67-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

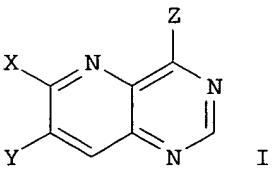


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:113672 HCAPLUS
DOCUMENT NUMBER: 130:182476
TITLE: Preparation of heterocyclic compounds as irreversible bicyclic inhibitors of tyrosine kinases
INVENTOR(S): Bridges, Alexander James
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906396	A1	19990211	WO 1998-US15592	19980729
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886659	A1	19990222	AU 1998-86659	19980729
US 6153617	A	20001128	US 1999-269647	19990325
US 2003087881	A1	20030508	US 2002-272651	20021017
PRIORITY APPLN. INFO.:			US 1997-54061P P	19970729
			WO 1998-US15592 W	19980729
			US 1999-269647 A3	19990325
			US 2000-656331 B1	20000906

OTHER SOURCE(S): MARPAT 130:182476
GI

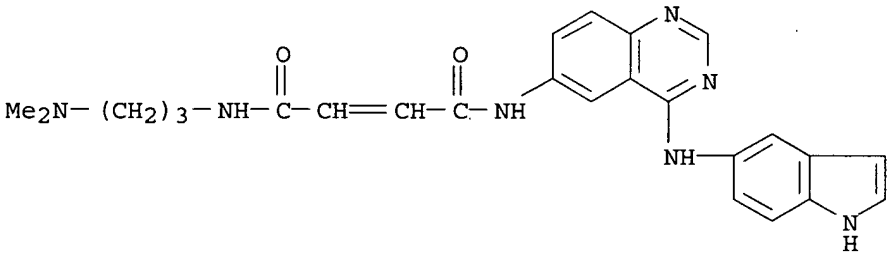


I

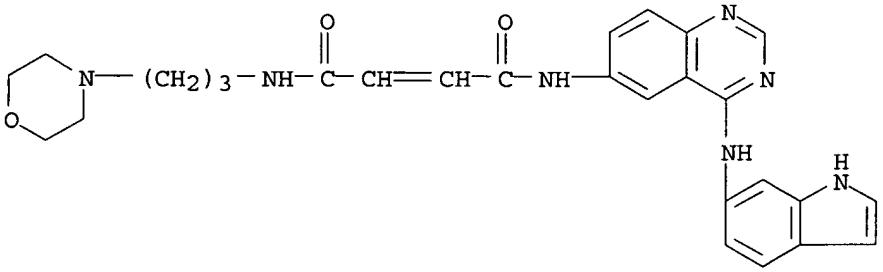
AB The title compds., e.g. I [X = DEF, Y = SR4, etc. ; or X = SR4, etc., and Y = DEF; D = O, etc.; E = CO, etc.; F = CR1(:C):C(R5)H, etc.; a proviso is given; R1 = H, halo, etc.; R5 = H, halo, perfluoroalkyl, etc.; Z = indoline moiety (generic structure given), etc.; R4 = H, alkyl, etc.], are prepared This invention also provides a method of treating cancer, restenosis, atherosclerosis, endometriosis, and psoriasis and a pharmaceutical composition that comprises a compound that is an irreversible inhibitor of tyrosine kinases. N-[4-(6-bromo-2,3-dihydroindol-1-yl)quinazolin-6-yl]acrylamide in vitro showed IC50 of 0.4 nM against epidermal growth factor receptor tyrosine kinase.

IT **220577-04-8P 220577-07-1P 220577-08-2P**
220577-11-7P 220577-12-8P 220578-04-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as irreversible bicyclic inhibitors of tyrosine kinases)

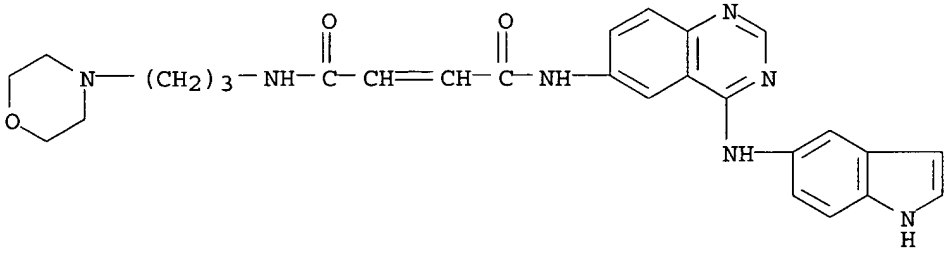
RN 220577-04-8 HCAPLUS
CN 2-Butenediamide, N-[3-(dimethylamino)propyl]-N'-[4-(1H-indol-5-ylamino)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



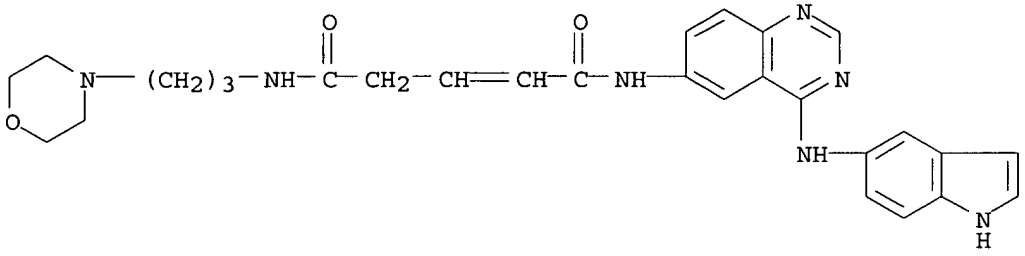
RN 220577-07-1 HCAPLUS
CN 2-Butenediamide, N-[4-(1H-indol-6-ylamino)-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



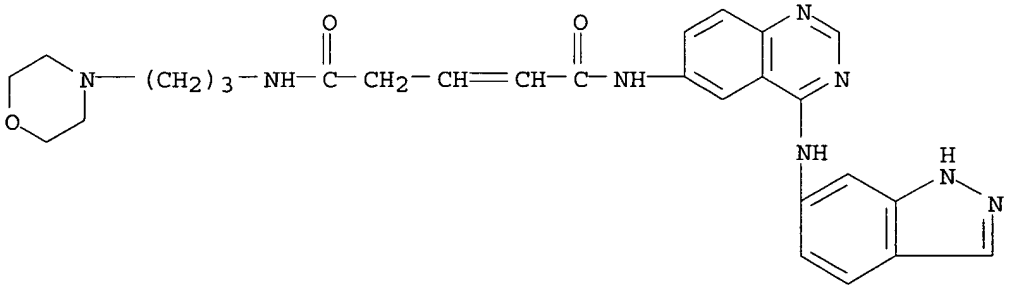
RN 220577-08-2 HCAPLUS
CN 2-Butenediamide, N-[4-(1H-indol-5-ylamino)-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



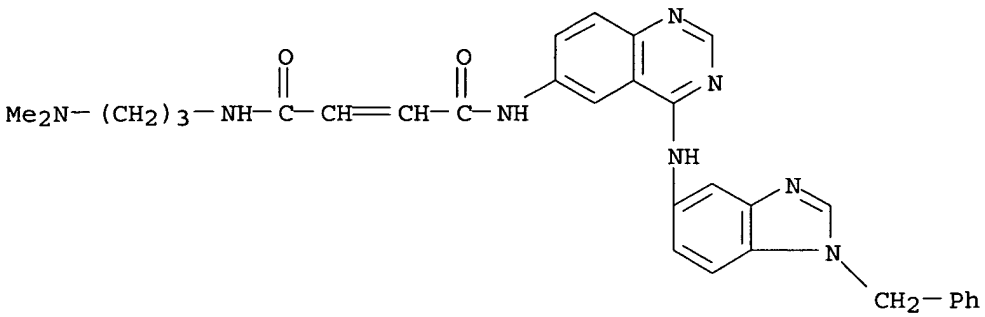
RN 220577-11-7 HCAPLUS
CN 2-Pentenediamide, N-[4-(1H-indol-5-ylamino)-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



RN 220577-12-8 HCAPLUS
CN 2-Pentenediamide, N-[4-(1H-indazol-6-ylamino)-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



RN 220578-04-1 HCAPLUS
CN 2-Butenediamide, N-[3-(dimethylamino)propyl]-N'-[4-[[1-(phenylmethyl)-1H-benzimidazol-5-yl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

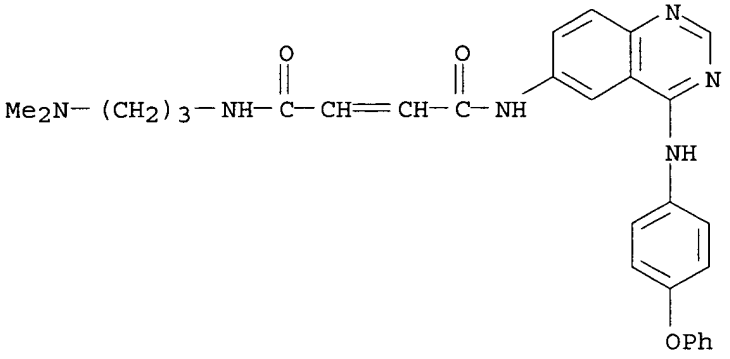
L8 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:113656 HCAPLUS
DOCUMENT NUMBER: 130:168387
TITLE: Irreversible inhibitors of tyrosine kinases
INVENTOR(S): Bridges, Alexander James
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906378	A1	19990211	WO 1998-US15784	19980729
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9887607	A1	19990222	AU 1998-87607	19980729
US 6127374	A	20001003	US 1999-269545	19990325
US 6562818	B1	20030513	US 2000-593031	20000613
PRIORITY APPLN. INFO.:			US 1997-54060P P	19970729
			WO 1998-US15784 W	19980729
			US 1999-269545 A3	19990325

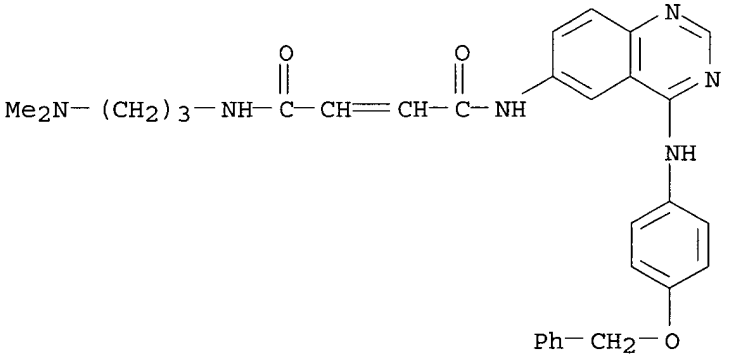
OTHER SOURCE(S): MARPAT 130:168387
AB Pyrimidine derivs. that are irreversible inhibitors of tyrosine kinases are reported. Thus, PhCH2OH was treated with 4-FC6H4NO2 to give 4-PhCH2OC6H4NO2, which was reduced to the amine and used to aminate 4-chloro-6-nitroquinazoline hydrochloride. The resulting 6-nitro-4-(4-benzyloxyanilino)quinazoline hydrochloride was reduced to the amine and acylated to give N-[4-(4-benzyloxyanilino)quinazolin-6-yl]acrylamide (I). I had an IC50 for inhibition of epidermal growth factor receptor tyrosine kinase of 3.6 nM.
IT **220488-58-4P 220488-59-5P 220488-62-0P**
220488-63-1P 220488-66-4P 220488-67-5P
220489-99-6P 220490-00-6P 220490-03-9P
220490-04-0P 220490-07-3P 220490-08-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(preparation of anilinoquinazolinylacrylamides and related compds. as tyrosine kinase inhibitors)

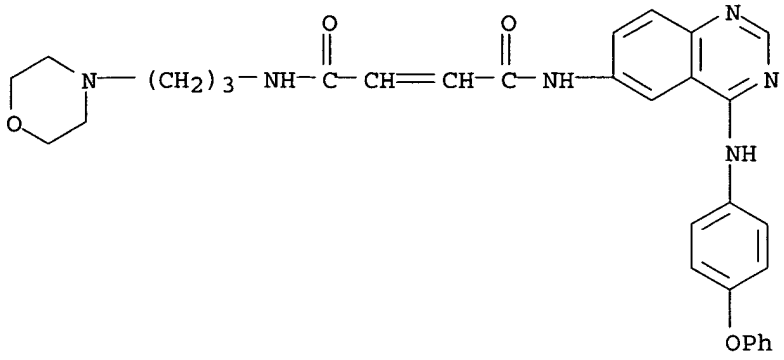
RN 220488-58-4 HCAPLUS
CN 2-Butenediamide, N-[3-(dimethylamino)propyl]-N'-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



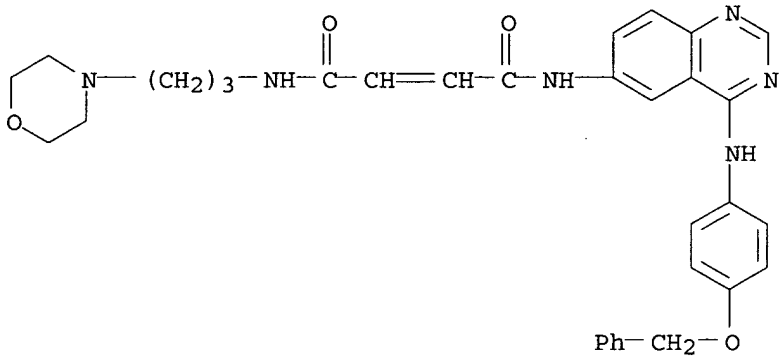
RN 220488-59-5 HCAPLUS
CN 2-Butenediamide, N-[3-(dimethylamino)propyl]-N'-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



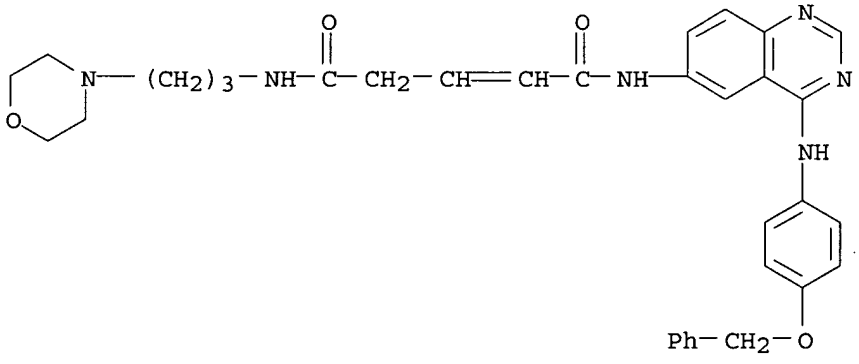
RN 220488-62-0 HCAPLUS
CN 2-Butenediamide, N-[3-(4-morpholinyl)propyl]-N'-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



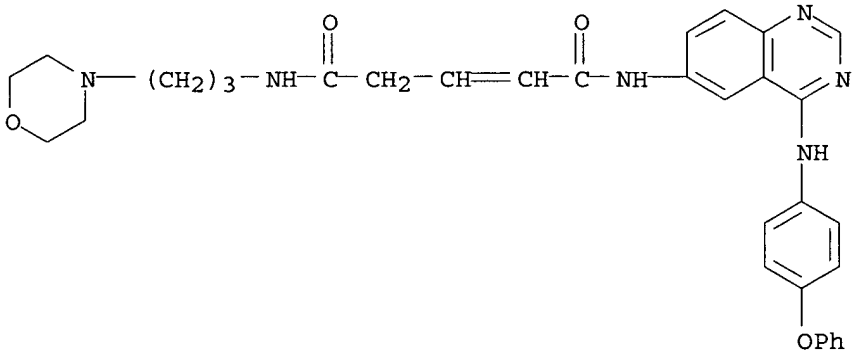
RN 220488-63-1 HCAPLUS
CN 2-Butenediamide, N-[3-(4-morpholinyl)propyl]-N'-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



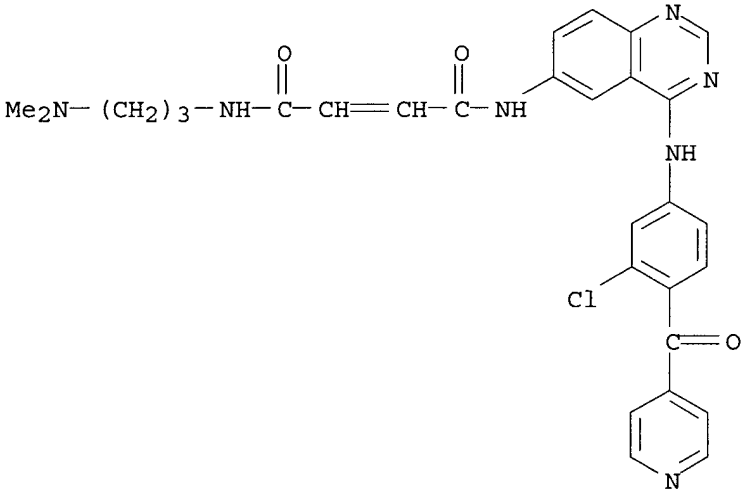
RN 220488-66-4 HCAPLUS
CN 2-Pentenediamide, N5-[3-(4-morpholinyl)propyl]-N1-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



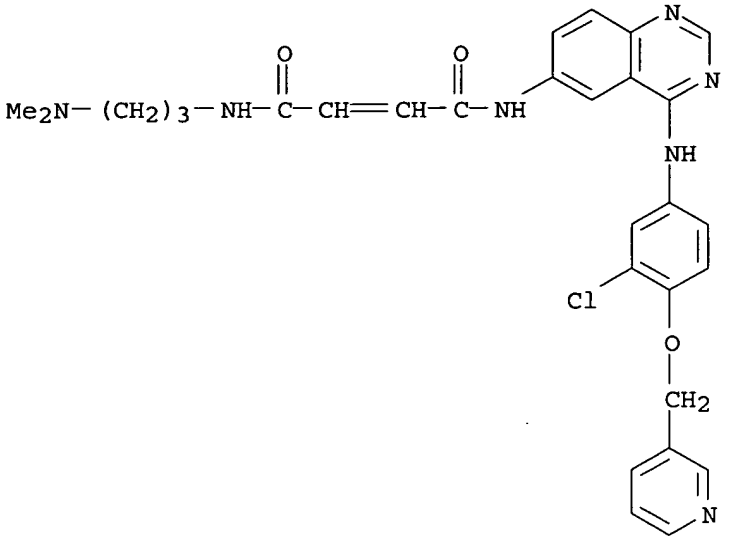
RN 220488-67-5 HCAPLUS
CN 2-Pentenediamide, N5-[3-(4-morpholinyl)propyl]-N1-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



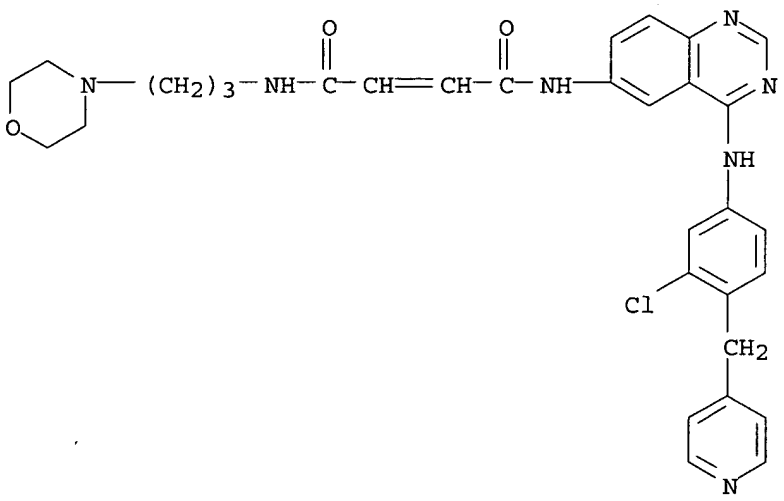
RN 220489-99-6 HCAPLUS
CN 2-Butenediamide, N-[4-[[3-chloro-4-(4-pyridinylcarbonyl)phenyl]amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



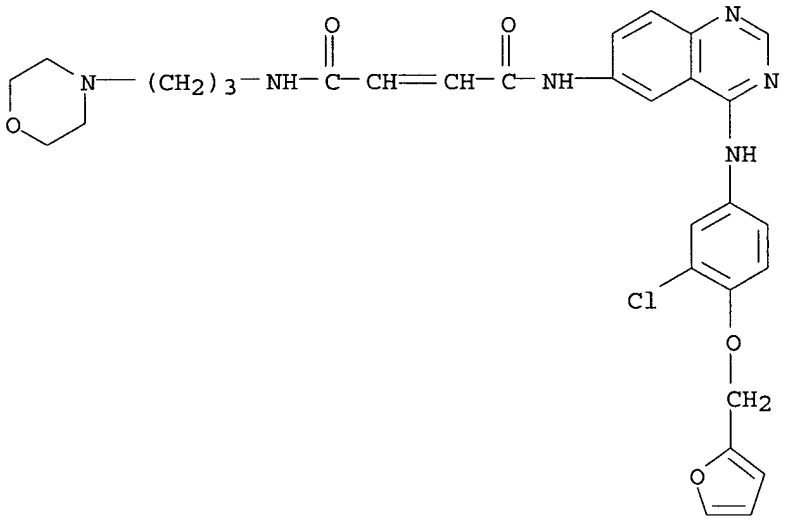
RN 220490-00-6 HCAPLUS
CN 2-Butenediamide, N-[4-[[3-chloro-4-(3-pyridinylmethoxy)phenyl]amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



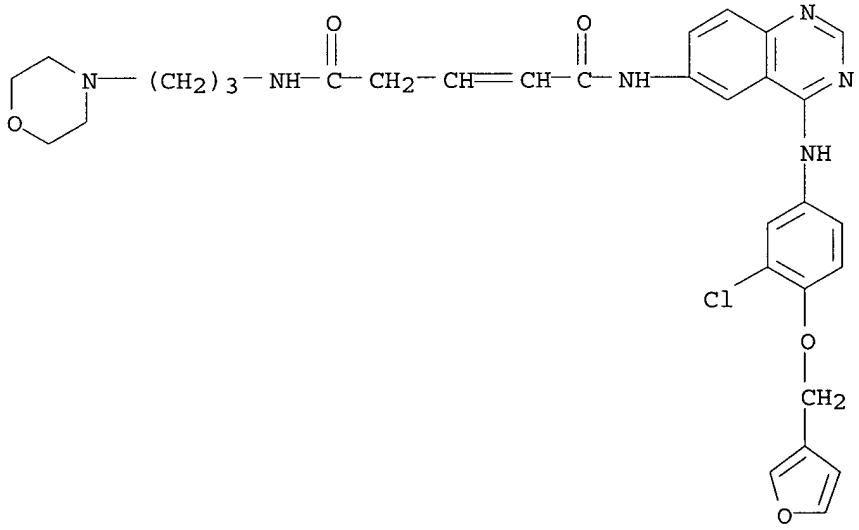
RN 220490-03-9 HCAPLUS
CN 2-Butenediamide, N-[4-[[3-chloro-4-(4-pyridinylmethyl)phenyl]amino]-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



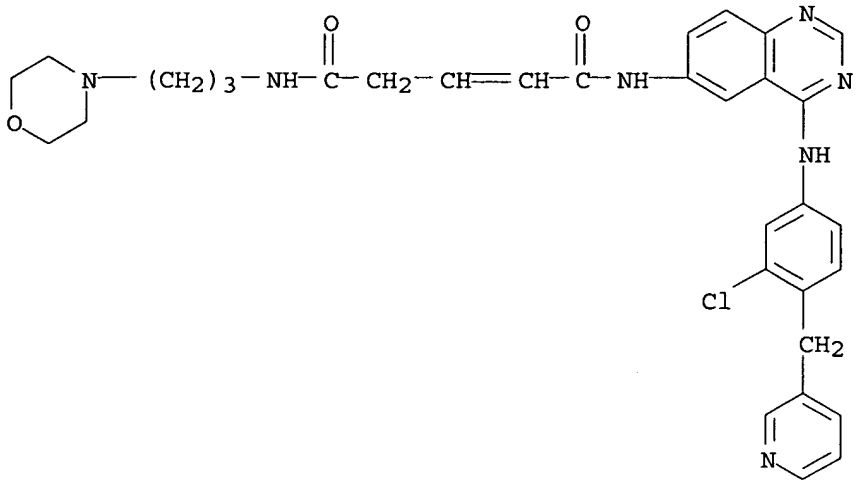
RN 220490-04-0 HCAPLUS
CN 2-Butenediamide, N-[4-[[3-chloro-4-(2-furanylmethoxy)phenyl]amino]-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



RN 220490-07-3 HCAPLUS
CN 2-Pentenediamide, N1-[4-[[3-chloro-4-(3-furanylmethoxy)phenyl]amino]-6-quinazolinyl]-N5-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



RN 220490-08-4 HCAPLUS
CN 2-Pentenediamide, N1-[4-[[3-chloro-4-(3-pyridinylmethyl)phenyl]amino]-6-quinazolinyl]-N5-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

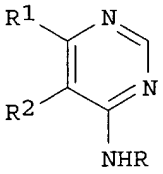
L8 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:696745 HCAPLUS
DOCUMENT NUMBER: 128:3695
TITLE: Preparation of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors
INVENTOR(S): Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong; et al.
PATENT ASSIGNEE(S): Warner-Lambert Company, USA; Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9738983	A1	19971023	WO 1997-US5778	19970408
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2249446	AA	19971023	CA 1997-2249446	19970408
AU 9724463	A1	19971107	AU 1997-24463	19970408
AU 725533	B2	20001012		
EP 892789	A1	19990127	EP 1997-920213	19970408
EP 892789	B1	20020227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

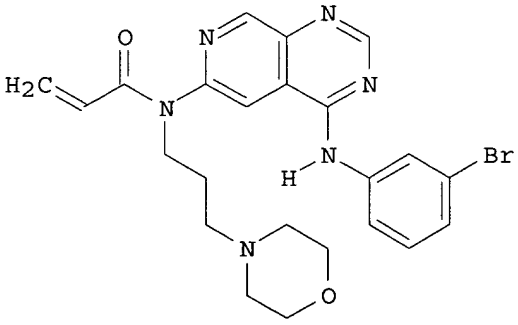
	IE, SI, LT, LV, FI				
	CN 1218456	A	19990602	CN 1997-194458	19970408
	CN 1145614	B	20040414		
	BR 9708640	A	19990803	BR 1997-8640	19970408
	JP 2000508657	T2	20000711	JP 1997-537173	19970408
	JP 3370340	B2	20030127		
	AT 213730	E	20020315	AT 1997-920213	19970408
	PT 892789	T	20020731	PT 1997-920213	19970408
	ES 2174250	T3	20021101	ES 1997-920213	19970408
	CN 1495172	A	20040512	CN 2003-10114126	19970408
	SK 284073	B6	20040908	SK 1998-1417	19970408
	CZ 295468	B6	20050817	CZ 1998-3244	19970408
	ZA 9703060	A	19971104	ZA 1997-3060	19970410
	BG 63160	B1	20010531	BG 1998-102811	19981001
	NO 9804718	A	19981209	NO 1998-4718	19981009
	NO 312588	B1	20020603		
	KR 2000005364	A	20000125	KR 1998-708086	19981010
	US 6344459	B1	20020205	US 1999-155501	19990608
	HK 1019739	A1	20050218	HK 1999-104872	19991028
	US 6602863	B1	20030805	US 2000-671559	20000927
	US 2003229051	A1	20031211	US 2003-441450	20030520
PRIORITY APPLN. INFO.:				US 1996-15351P	P 19960412
				WO 1997-US5778	W 19970408
				US 1999-155501	A3 19990608
				US 2000-671559	A3 20000927

OTHER SOURCE(S): MARPAT 128:3695

GI



I



II

AB Title compds. [I; R = (CHR6)pR9; R1R2 = CH:CR7CR8:CH, CH:CR7CR8:N, CH:CR7N:CH, etc.; R6 = H or alkyl; 1 of R7,R8 = Z1Z2R10 and the other = OR4, SR4, NHR3; R3,R4 = (un)substituted alkyl, heterocyclylalkyl, etc.; R9 = (un)substituted Ph; R10 = CR11:CHR5, C.tplbond.CR5, CR11:C:CHR5; R5 = H, halo, alkyl, Ph, etc.; R11 = H, halo, alkyl; Z1 = bond, O, (alkyl)imino, CH2, etc.; Z2 = CO, SO, P(O)(OH), etc.; p = 0 or 1] were prepared Thus, I (R = C6H4Br-3, R1R2 = CH:NCR8:CH, R8 = F) was condensed with 3-morpholinoprpanamine and the product acylated by CH2:CHCOCl to give title compound II. Data for biol. activity of I were given.

IT **198960-34-8P 198960-63-3P 198960-87-1P**
198960-89-3P 198960-91-7P 198960-93-9P
198961-22-7P 198961-24-9P 198961-25-0P
198961-27-2P 198961-29-4P 198961-31-8P
198961-36-3P 198961-37-4P 198961-39-6P

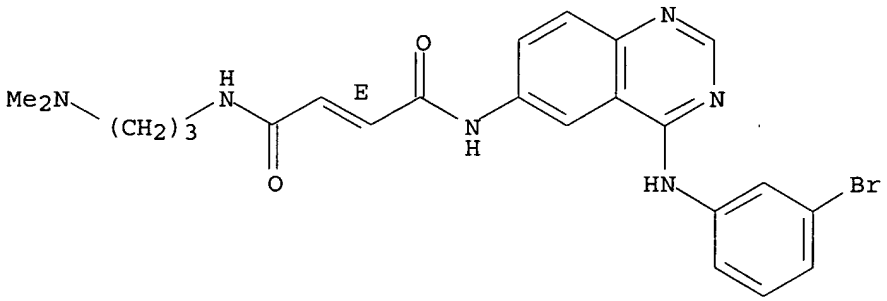
198961-42-1P 198961-43-2P 198961-45-4P
198961-46-5P 198961-48-7P 198961-52-3P
198961-55-6P 198961-61-4P 198961-62-5P
198961-64-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors)

RN 198960-34-8 HCAPLUS
CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]-, (2E)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

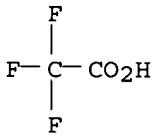
CRN 198960-33-7
CMF C23 H25 Br N6 O2

Double bond geometry as shown.

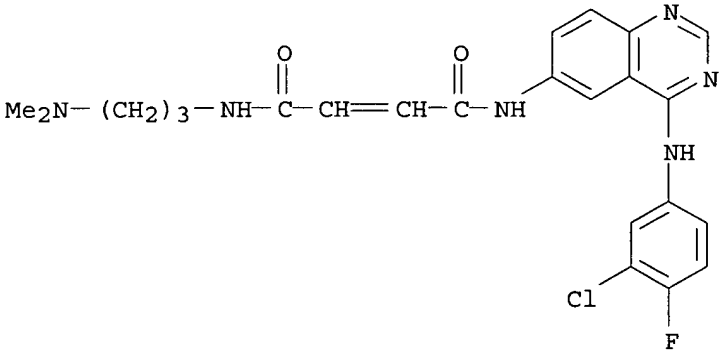


CM 2

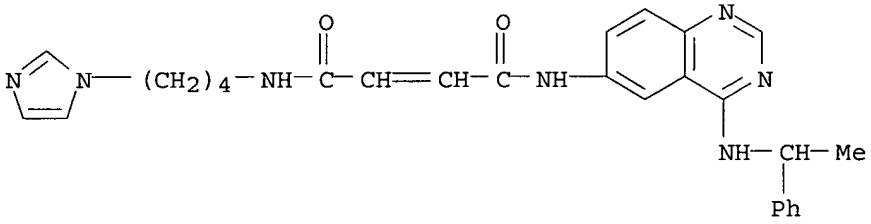
CRN 76-05-1
CMF C2 H F3 O2



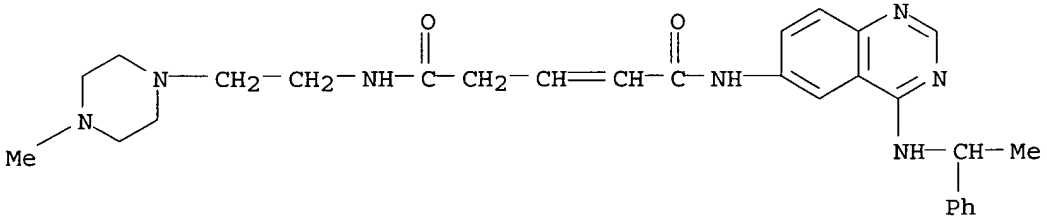
RN 198960-63-3 HCAPLUS
CN 2-Butenediamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



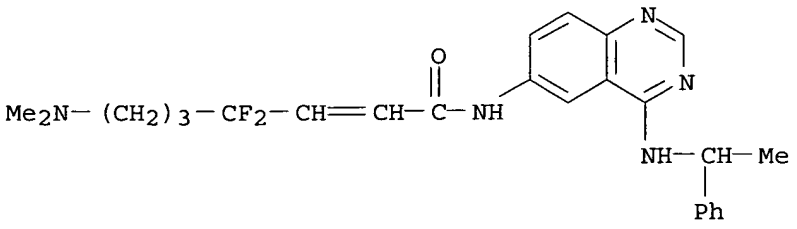
RN 198960-87-1 HCAPLUS
CN 2-Butenediamide, N-[4-(1H-imidazol-1-yl)butyl]-N'-[4-[(1-phenylethyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



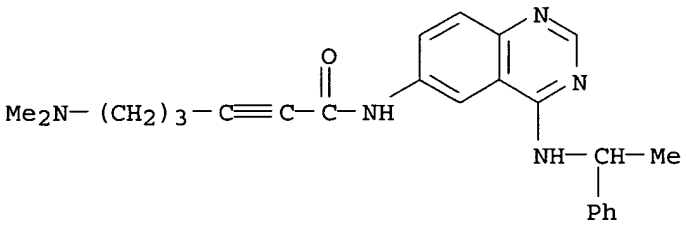
RN 198960-89-3 HCAPLUS
CN 2-Pentenediamide, N5-[2-(4-methyl-1-piperazinyl)ethyl]-N1-[4-[(1-phenylethyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



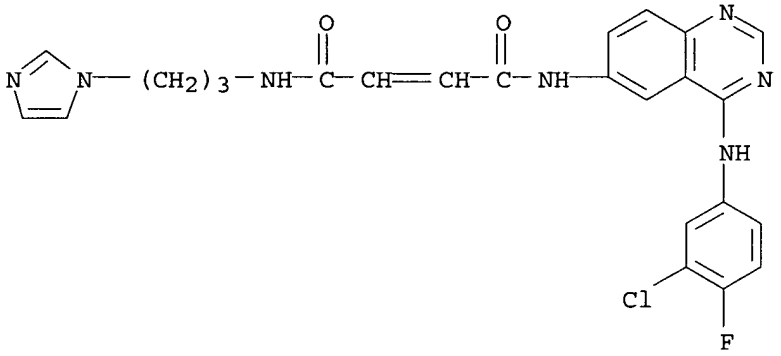
RN 198960-91-7 HCAPLUS
CN 2-Heptenamide, 7-(dimethylamino)-4,4-difluoro-N-[4-[(1-phenylethyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



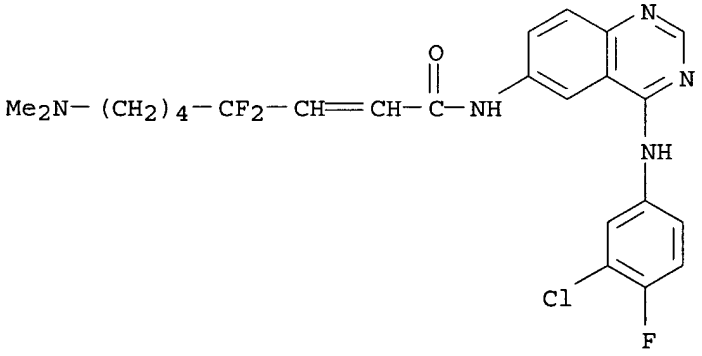
RN 198960-93-9 HCAPLUS
CN 2-Hexynamide, 6-(dimethylamino)-N-[4-[(1-phenylethyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



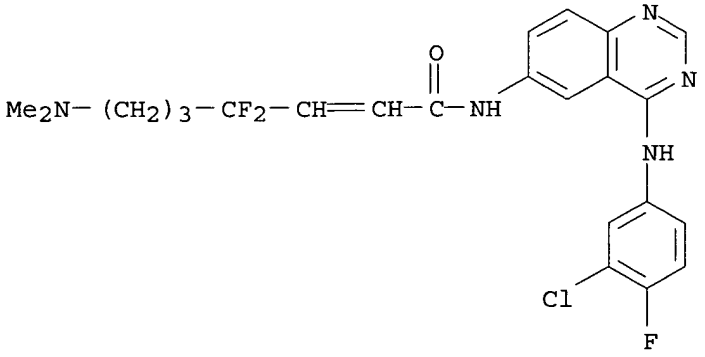
RN 198961-22-7 HCAPLUS
CN 2-Butenediamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N'-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



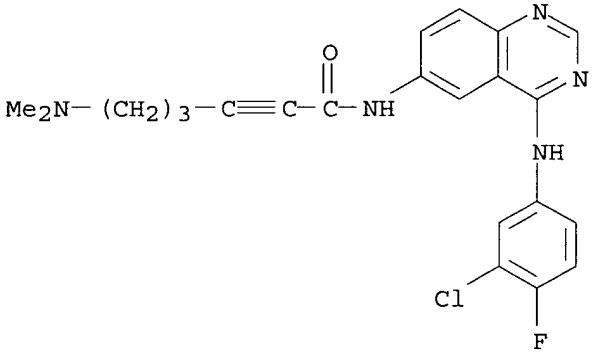
RN 198961-24-9 HCAPLUS
CN 2-Octenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-8-(dimethylamino)-4,4-difluoro- (9CI) (CA INDEX NAME)



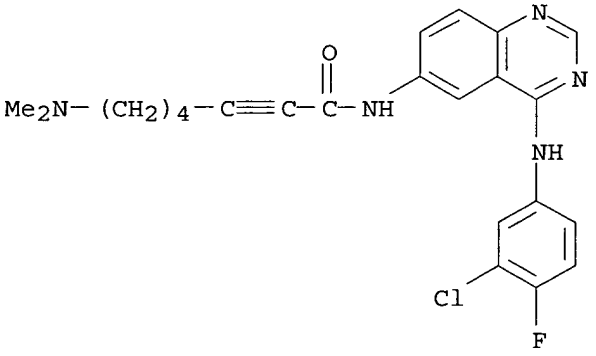
RN 198961-25-0 HCAPLUS
CN 2-Heptenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-7-(dimethylamino)-4,4-difluoro- (9CI) (CA INDEX NAME)



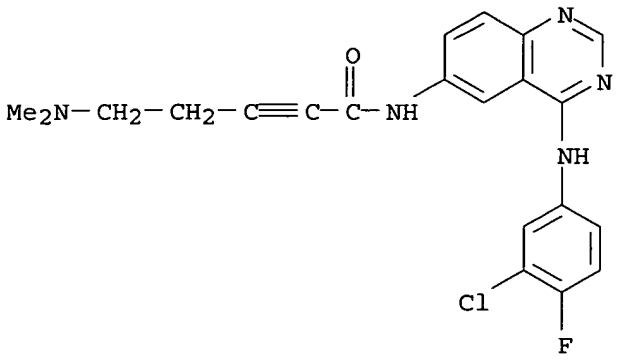
RN 198961-27-2 HCAPLUS
CN 2-Hexynamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-6-(dimethylamino)- (9CI) (CA INDEX NAME)



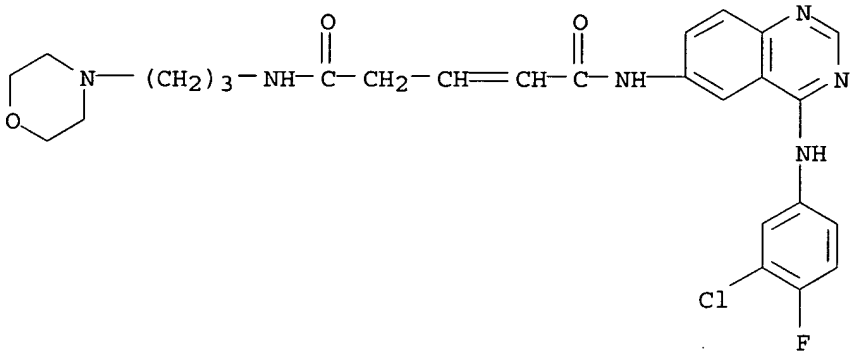
RN 198961-29-4 HCAPLUS
CN 2-Heptynamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-7-(dimethylamino)- (9CI) (CA INDEX NAME)



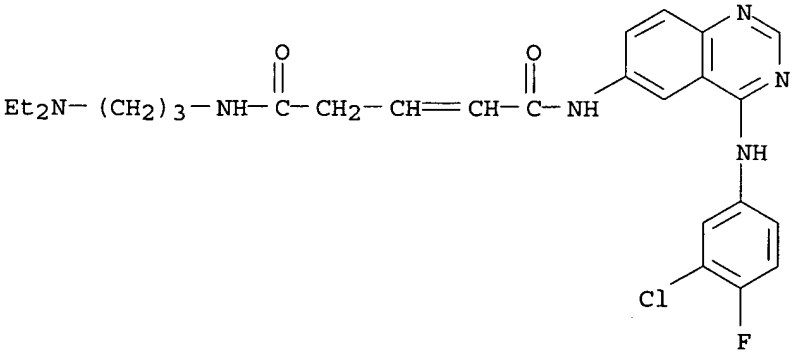
RN 198961-31-8 HCAPLUS
CN 2-Pentynamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-5-(dimethylamino)- (9CI) (CA INDEX NAME)



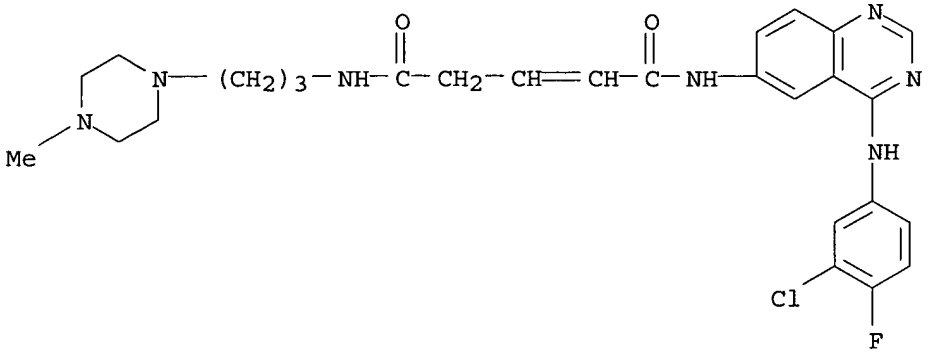
RN 198961-36-3 HCAPLUS
CN 2-Pentenediamide, N1-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N5-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



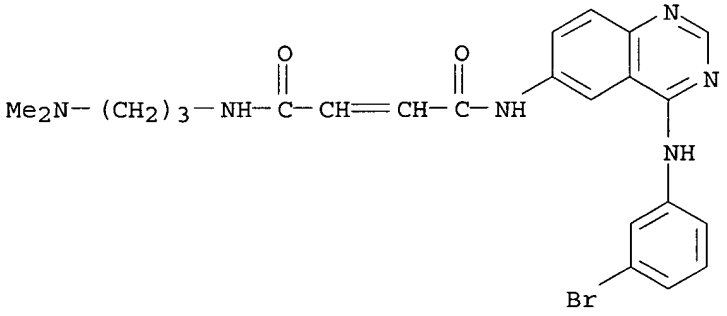
RN 198961-37-4 HCAPLUS
CN 2-Pentenediamide, N1-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N5-[3-(diethylamino)propyl]- (9CI) (CA INDEX NAME)



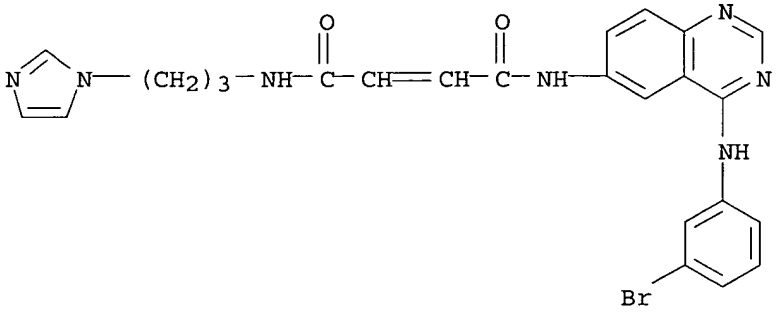
RN 198961-39-6 HCAPLUS
CN 2-Pentenediamide, N1-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N5-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



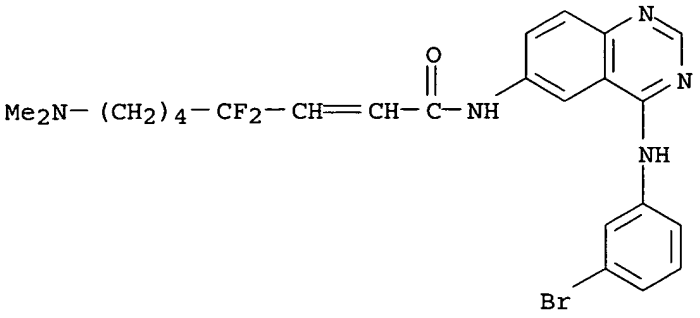
RN 198961-42-1 HCAPLUS
CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



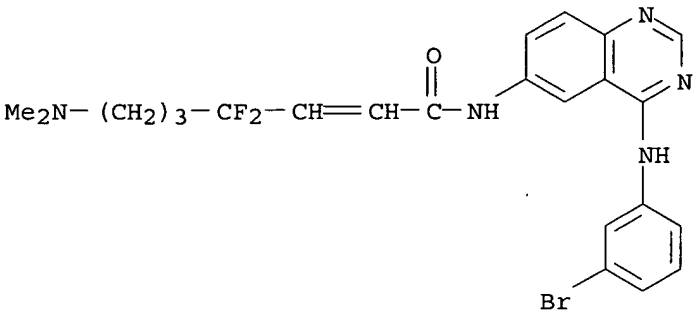
RN 198961-43-2 HCAPLUS
CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



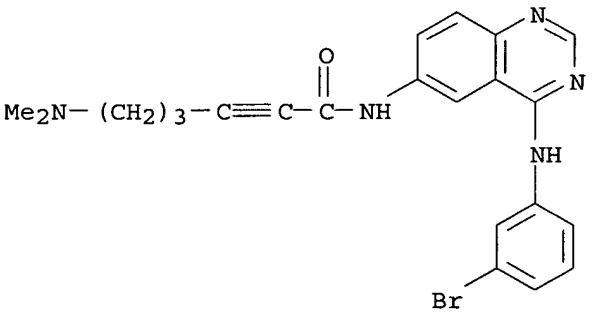
RN 198961-45-4 HCAPLUS
CN 2-Octenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-8-(dimethylamino)-4,4-difluoro- (9CI) (CA INDEX NAME)



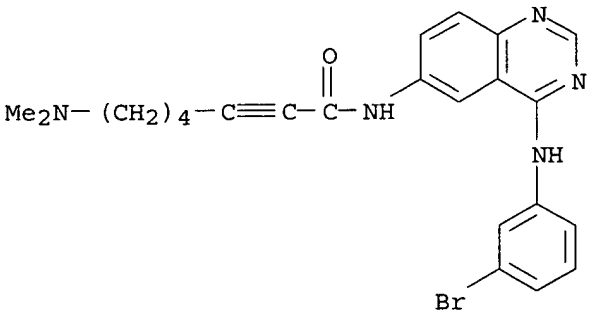
RN 198961-46-5 HCAPLUS
CN 2-Heptenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-7-(dimethylamino)-4,4-difluoro- (9CI) (CA INDEX NAME)



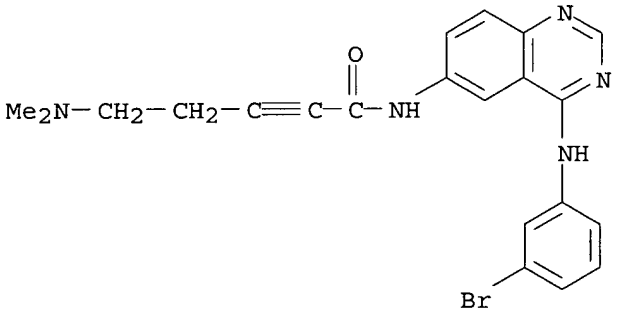
RN 198961-48-7 HCAPLUS
CN 2-Hexynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-6-(dimethylamino)- (9CI) (CA INDEX NAME)



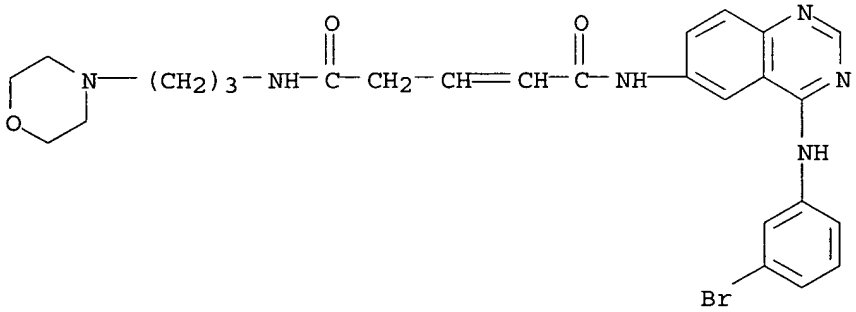
RN 198961-52-3 HCAPLUS
CN 2-Heptynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-7-(dimethylamino)- (9CI) (CA INDEX NAME)



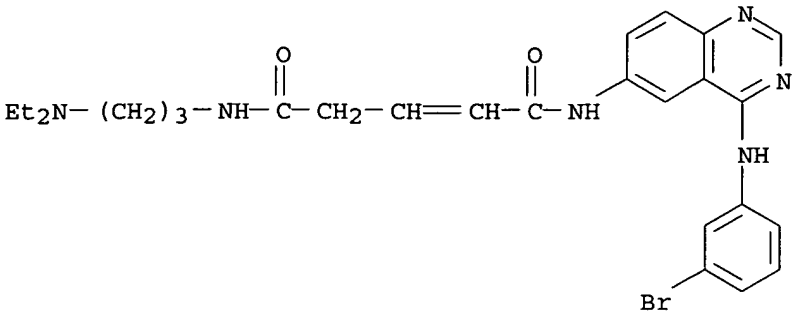
RN 198961-55-6 HCAPLUS
CN 2-Pentynamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-5-(dimethylamino)- (9CI) (CA INDEX NAME)



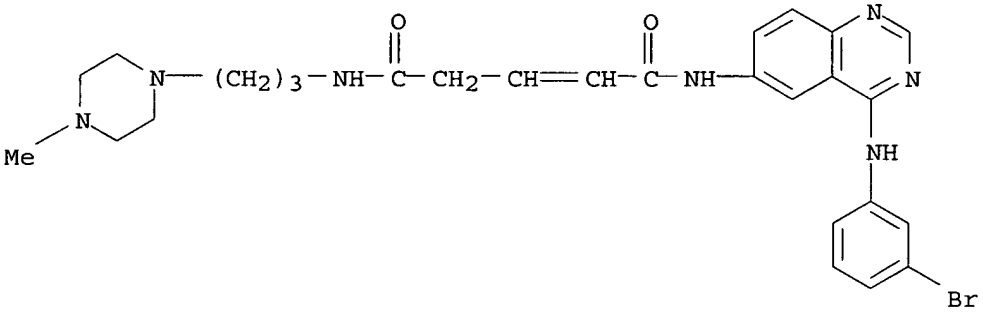
RN 198961-61-4 HCAPLUS
CN 2-Pentenediamide, N1-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N5-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



RN 198961-62-5 HCAPLUS
CN 2-Pentenediamide, N1-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N5-[3-(diethylamino)propyl]- (9CI) (CA INDEX NAME)



RN 198961-64-7 HCAPLUS
CN 2-Pentenediamide, N1-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N5-[3-(4-methyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



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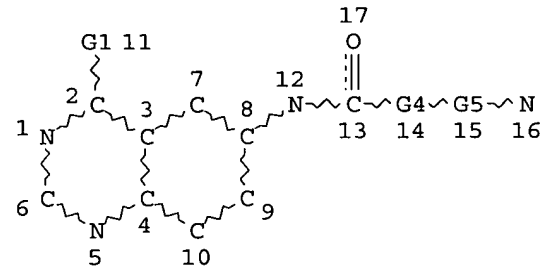
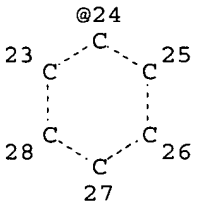
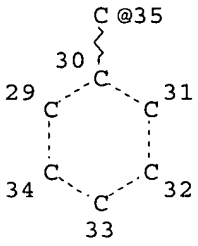
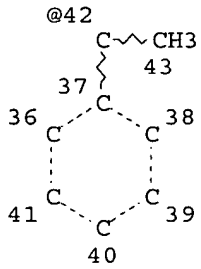
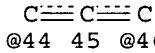
L3 STR

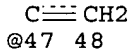


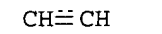


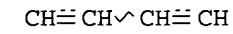












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VAR G2=24/35/42
VAR G3=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
VAR G4=44-13 46-15/47/49-13 50-15/51-13 52-15/53-13 56-15/C
REP G5=(1-9) C
NODE ATTRIBUTES:
NSPEC IS RC AT 16
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE
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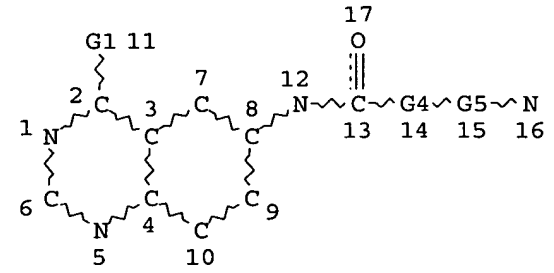
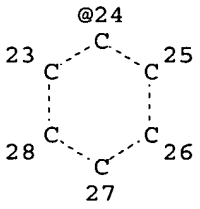
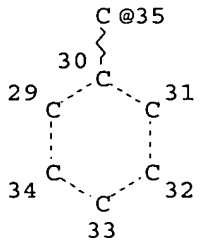
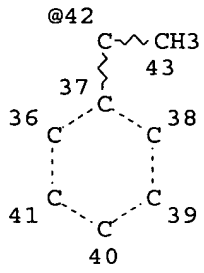
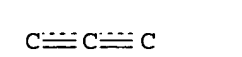
L6 STR

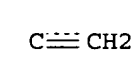


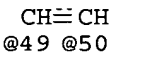


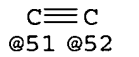


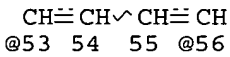












VAR G1=18/21
VAR G2=24/35/42
VAR G3=ME/ET/I-PR/N-PR/I-BU/N-BU/T-BU/S-BU
VAR G4=44-13 46-15/47/49-13 50-15/51-13 52-15/53-13 56-15/C
REP G5=(1-9) C
NODE ATTRIBUTES:
NSPEC IS C AT 16
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 56

STEREO ATTRIBUTES: NONE
L7 214 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L8 32 SEA FILE=HCAPLUS ABB=ON PLU=ON L7
L9 240 SEA FILE=REGISTRY ABB=ON PLU=ON L5 NOT L7
L10 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L9
L11 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 NOT L8

=>
=>

=> d ibib abs hitstr l11 1-3

L11 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:719893 HCAPLUS
DOCUMENT NUMBER: 141:243560
TITLE: Preparation of 4-anilinoquinazolines as tyrosine kinase inhibitors for the treatment of tumors

INVENTOR(S): Himmelsbach, Frank; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: Ger. Offen., 21 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10307165	A1	20040902	DE 2003-10307165	20030220
US 2005107358	A1	20050519	US 2004-778985	20040213
WO 2004074263	A1	20040902	WO 2004-EP1398	20040214

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI, NI, NO
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2003-10307165 A 20030220
US 2003-452280P P 20030305

OTHER SOURCE(S): MARPAT 141:243560
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

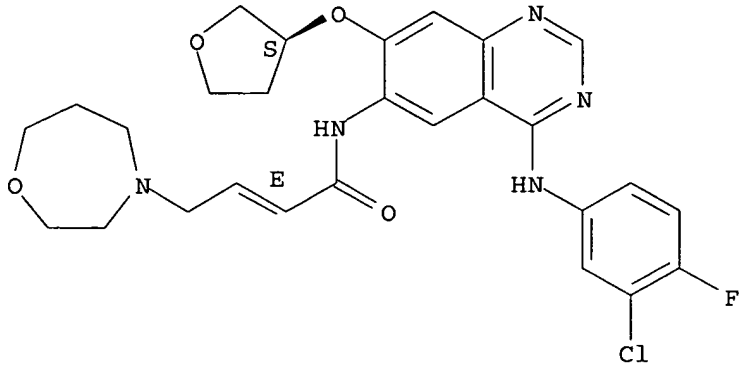
AB Title compds. I [R1 = H, alkyl; R2 = (un)substituted Ph, benzyl, 1-phenylethyl; R3 = H, halo, OH, etc.; R4, R5 = H, alkyl; X = C(CN), N with provisos; Z = (un)substituted heterocycle] and their pharmaceutically acceptable salts ands formulations were prepared For example, coupling of 4-[2,2-dimethoxyethyl]homomorpholine and phosphonate II, e.g., prepared from di-Et carboxymethylphosphonate and N4-(3-chloro-4-fluorophenyl)-7-[[(3S)-tetrahydro-3-furanyl]oxy]-4,6-quinazolinediamine, afforded claimed anilinoquinazoline III in 63% yield. In human epidermal growth factor receptor binding assays, anilinoquinazoline III exhibited an IC50 value of 1.5 nM. Compds. I are claimed useful for the treatment of tumors, i.e, prostate benign hyperplasia.

IT **749879-39-8P 749879-40-1P 749879-41-2P**
749879-42-3P 749879-43-4P 749879-44-5P
749879-45-6P 749879-46-7P 749879-47-8P
749879-48-9P 749879-49-0P 749879-50-3P
749879-51-4P 749879-52-5P 749879-53-6P
749879-54-7P 749879-55-8P 749879-56-9P
749879-57-0P 749879-58-1P 749879-59-2P
749879-60-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-anilinoquinazolines as tyrosine kinase inhibitors for the treatment of tumors)

RN 749879-39-8 HCAPLUS

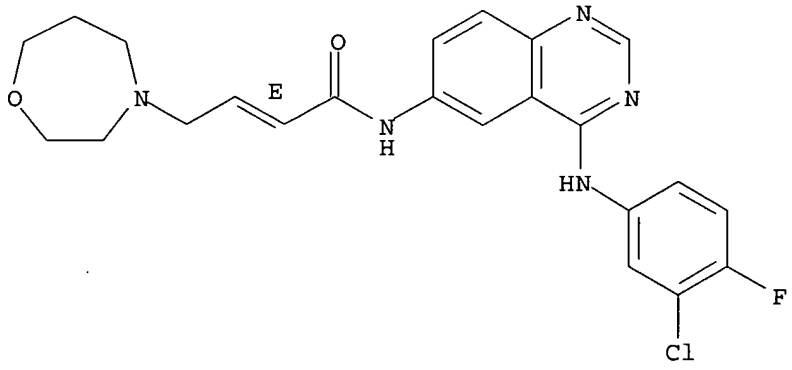
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



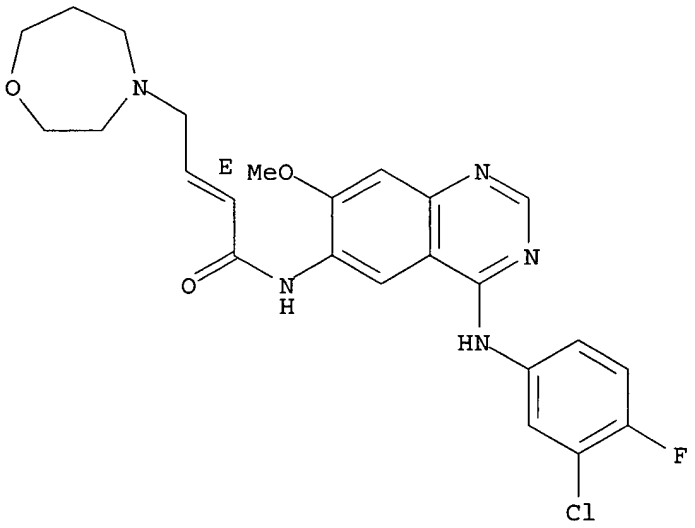
RN 749879-40-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



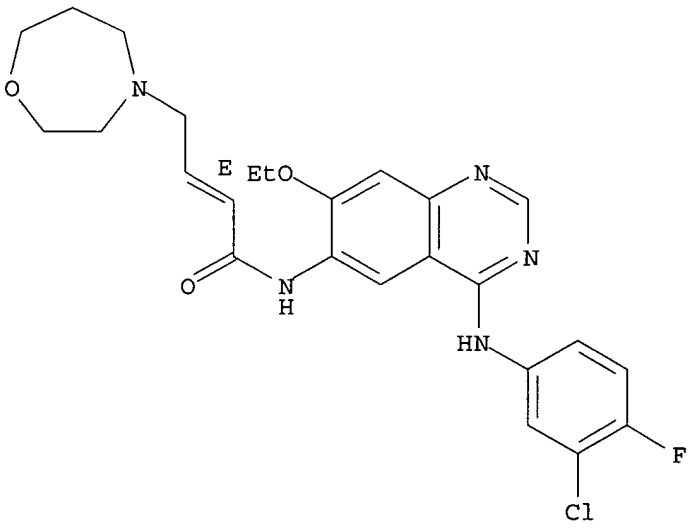
RN 749879-41-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



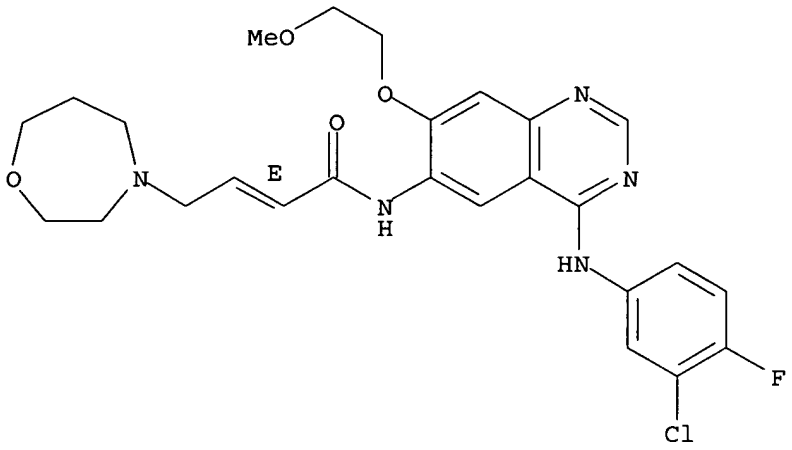
RN 749879-42-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-ethoxy-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



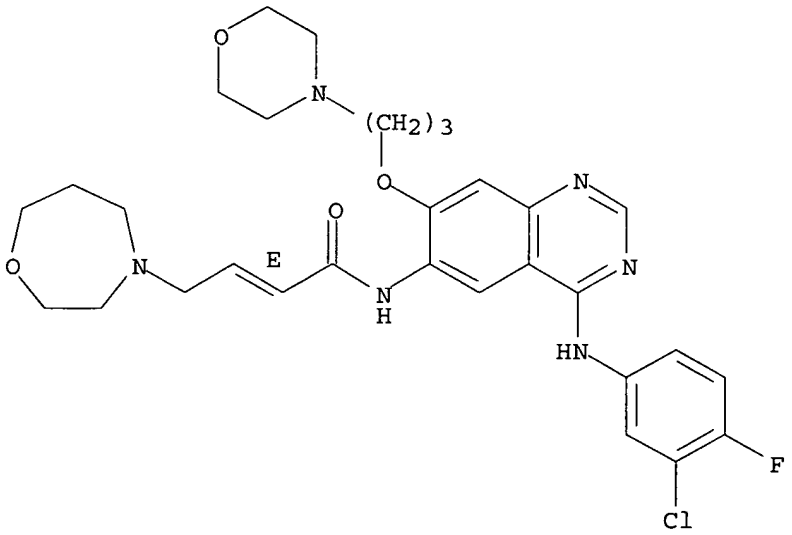
RN 749879-43-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(2-methoxyethoxy)-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



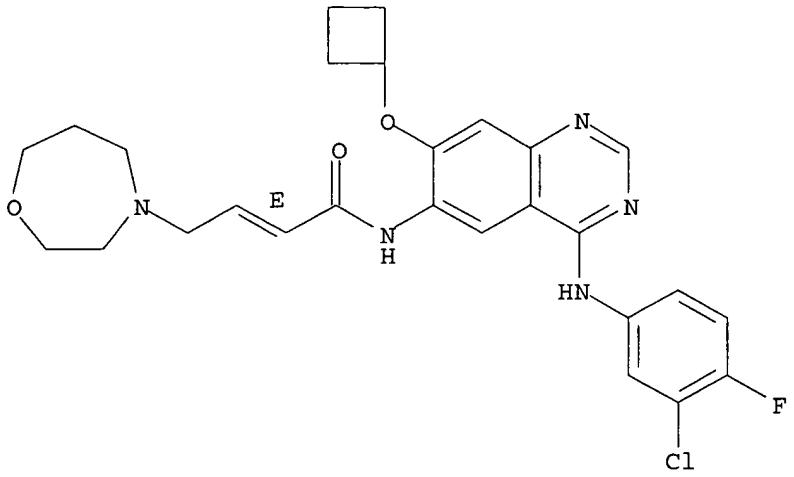
RN 749879-44-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(4-morpholinyl)propoxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



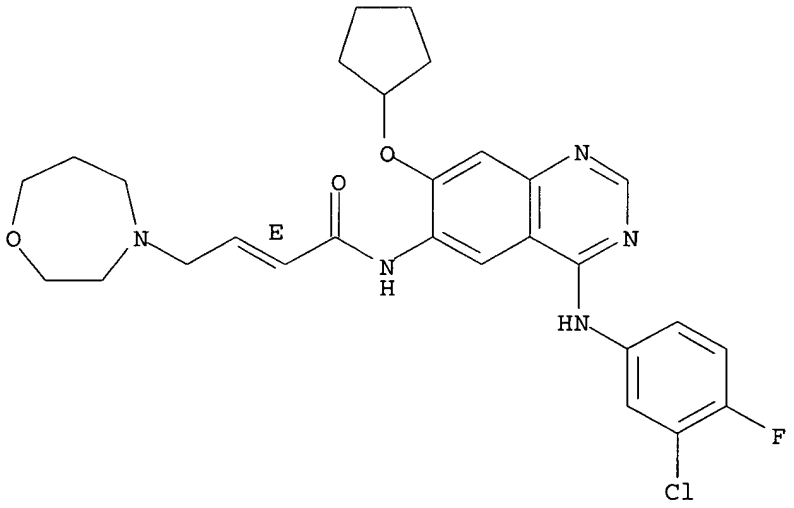
RN 749879-45-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



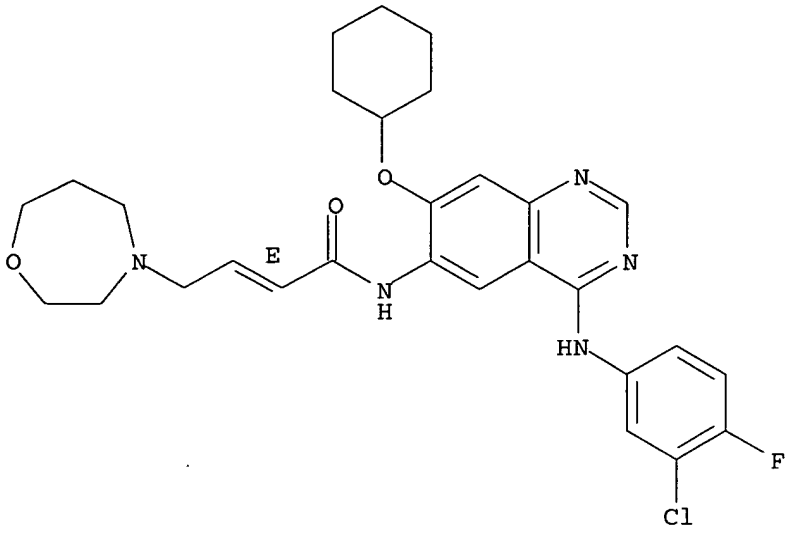
RN 749879-46-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



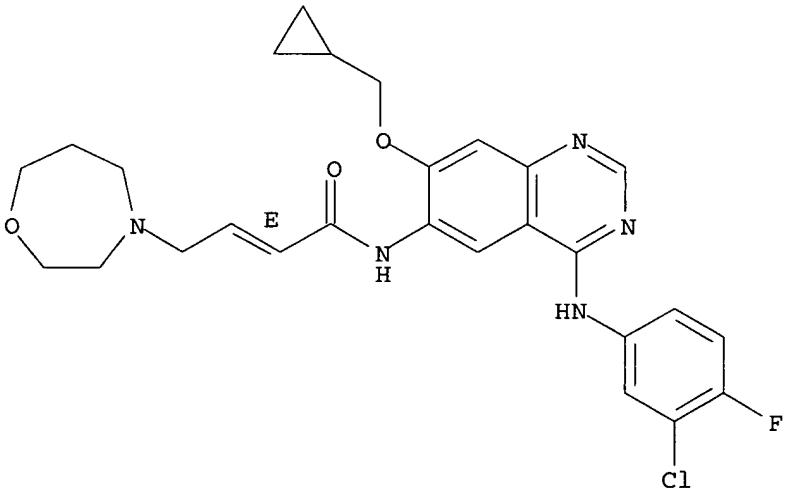
RN 749879-47-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclohexyloxy)-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



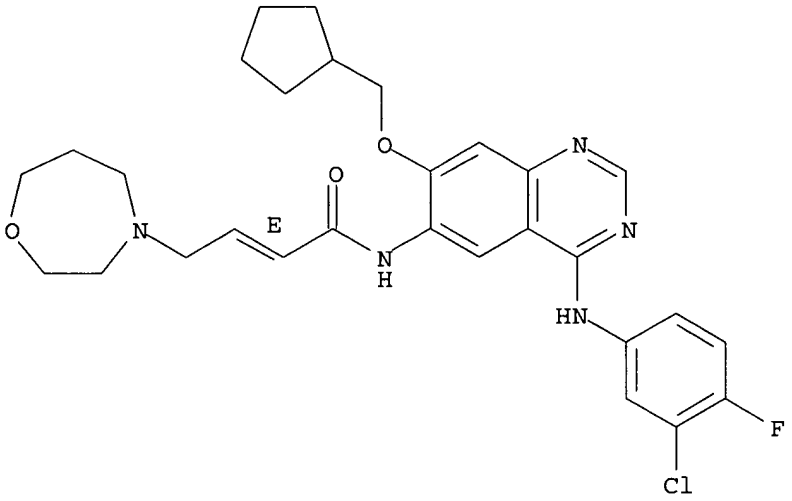
RN 749879-48-9 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



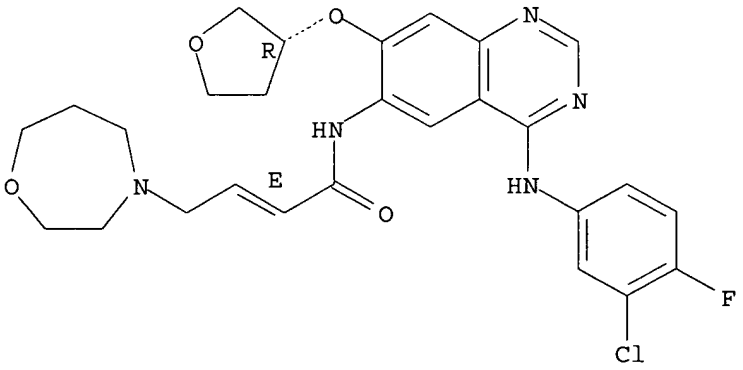
RN 749879-49-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentylmethoxy)-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



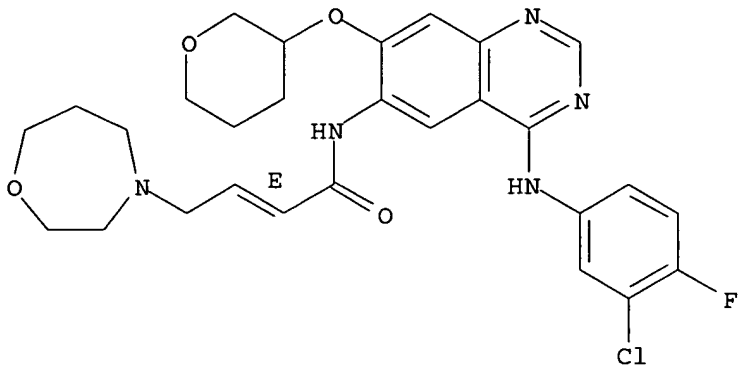
RN 749879-50-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



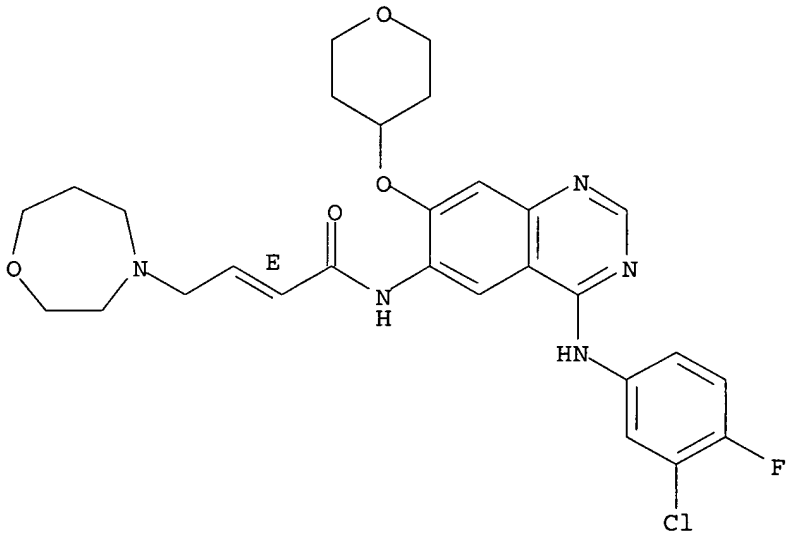
RN 749879-51-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-3-yl)oxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



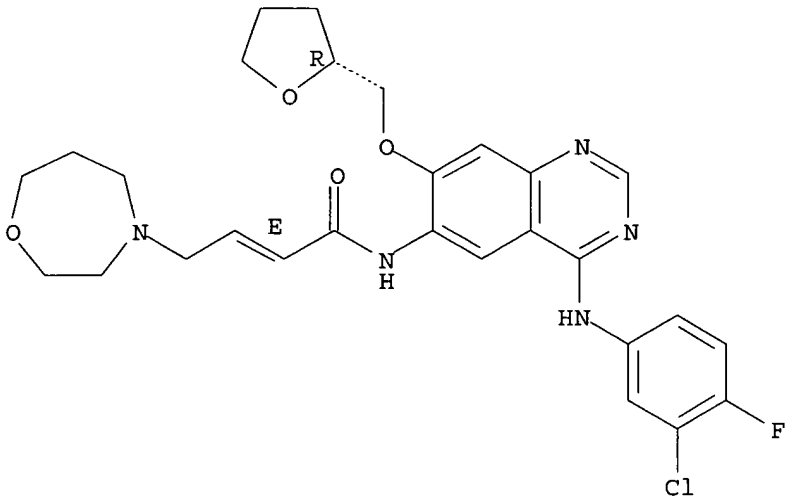
RN 749879-52-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



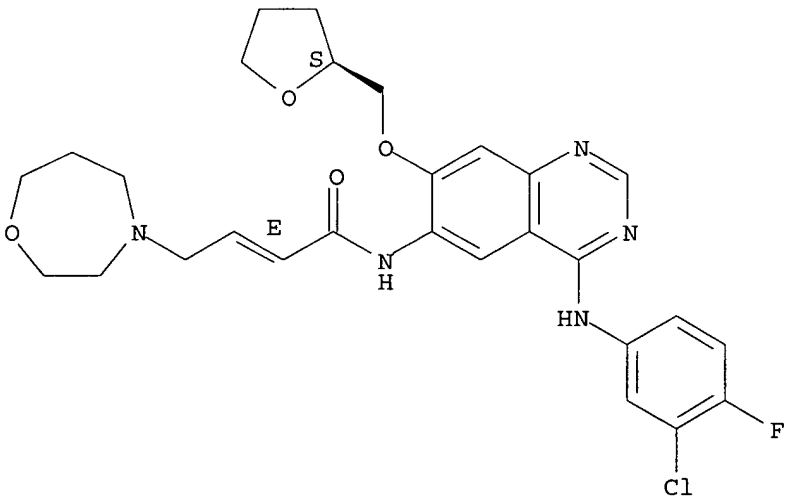
RN 749879-53-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



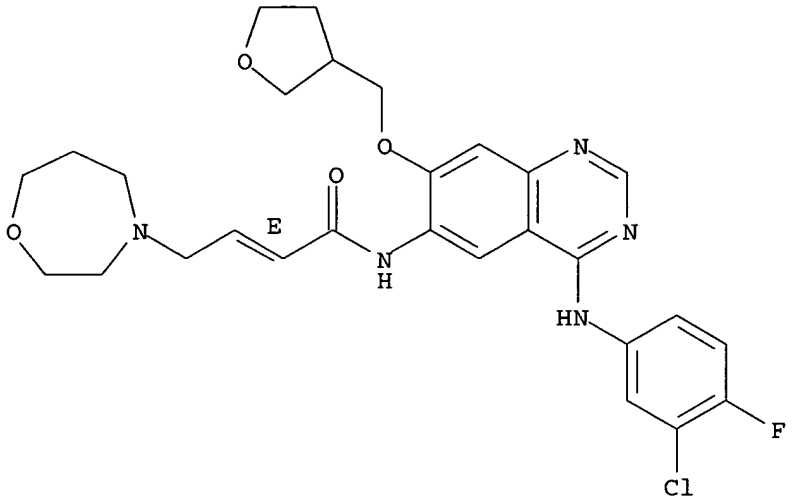
RN 749879-54-7 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



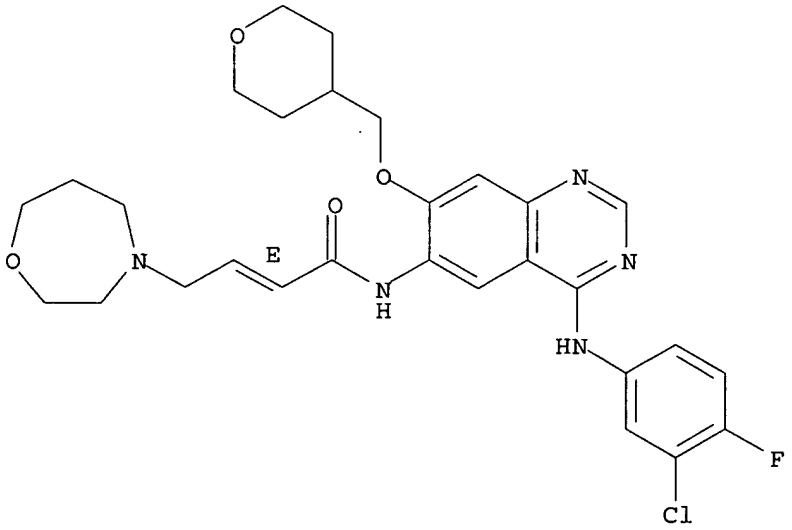
RN 749879-55-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



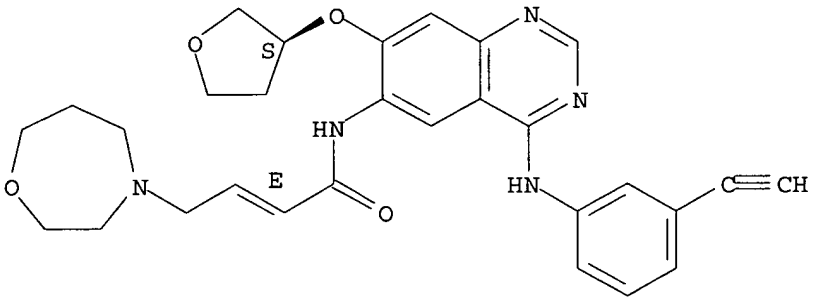
RN 749879-56-9 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



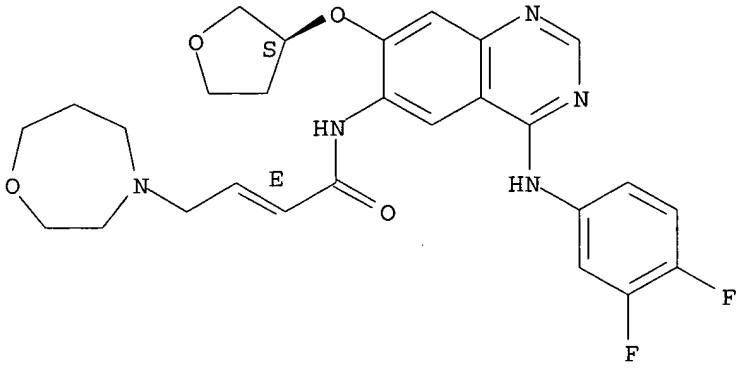
RN 749879-57-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-ethynylphenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



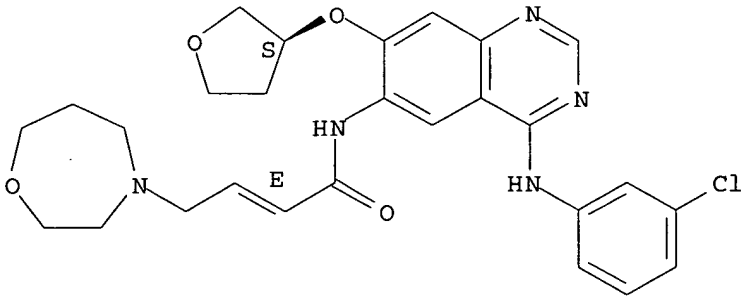
RN 749879-58-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3,4-difluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 749879-59-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chlorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)-(9CI) (CA INDEX NAME)

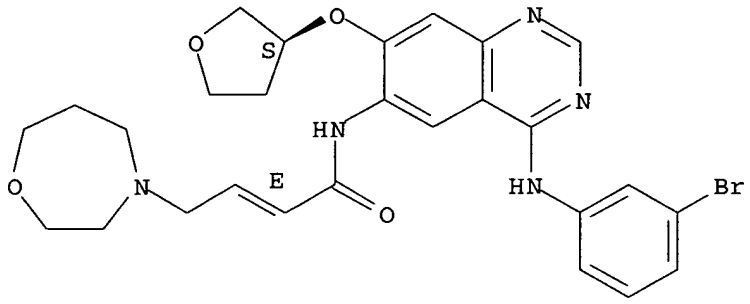
Absolute stereochemistry.
Double bond geometry as shown.



RN 749879-60-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-[[(3S)-tetrahydro-3-

furanyl]oxy]-6-quinazolinyl]-4-(tetrahydro-1,4-oxazepin-4(5H)-yl)-, (2E)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

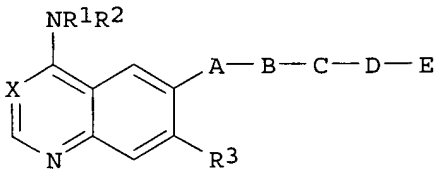


L11 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:855936 HCAPLUS
DOCUMENT NUMBER: 139:350749
TITLE: Preparation of 4-aminoquinazolines as inhibitors of epidermal growth factor receptor (EGF-R)
INVENTOR(S): Himmelsbach, Frank; Jung, Birgit; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089439	A1	20031030	WO 2003-EP3828	20030414
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10217689	A1	20031113	DE 2002-10217689	20020419
CA 2484395	AA	20031030	CA 2003-2484395	20030414
EP 1499619	A1	20050126	EP 2003-746824	20030414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526837	T2	20050908	JP 2003-586159	20030414
US 2004044014	A1	20040304	US 2003-417647	20030417
US 2005159436	A1	20050721	US 2005-81067	20050315

PRIORITY APPLN. INFO.:		
DE 2002-10217689	A	20020419
US 2002-387021P	P	20020607
WO 2003-EP3828	W	20030414
US 2003-417647	B1	20030417

OTHER SOURCE(S): MARPAT 139:350749
GI



I

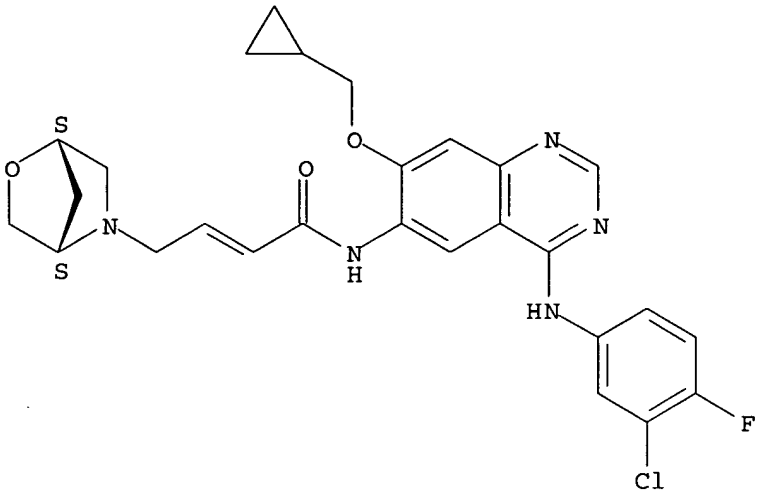
AB Title compds. [I; R1 = H, alkyl; R2 = Ph, benzyl, 1-phenylethyl in which Ph is substituted; R3 = H, F, Cl, Br, OH, alkoxy, fluorinated OMe, OEt, substituted alkoxy; cycloalkyloxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, etc.; A = imino, alkylimino, B = CO, SO2; C = (substituted) 1,3-allenylene, 1,1-vinylene, 1,2-vinylene, C.tplbond.CH, etc.; D = (branched) alkylene; E = bridged pyrrolidin-1-yl, piperidin-1-yl, piperazin-1-yl, morpholin-4-yl] tautomers, stereoisomers, mixts. and salts thereof, particularly their physiol. compatible salts with inorg. or organic acids, were prepared Thus, a solution of LiCl in H2O was treated with 4-[(3-chloro-4-fluorophenyl)amino]-6-[2-(diethoxyphosphoryl)acetylamino]-7-[(S)-(tetrahydrofuran-3-yl)oxy]quinazoline (preparation given) in THF followed by addition of KOH-pellets and cooling at -3°. Then, the reaction mixture was dropwise treated with (1S,4S)-(2-oxa-5-azabicyclo[2.2.1]hept-5-yl)acetaldehyde hydrochloride (preparation given) for 5 min at 0° followed by stirring for 10 min at 0° and for 20 min at room temperature to give 60% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl]-1-oxo-2-buten-1-yl)amino]-7-[(S)-(tetrahydrofuran-3-yl)oxy]quinazoline. The latter inhibited EGF-receptor kinase with IC50 = 0.5 nM. The invention also relates to the use of these compds. for treating diseases, particularly tumor diseases and benign prostatic hyperplasia (BPH), diseases of the lungs and of the respiratory tract.

IT **618061-81-7P 618061-83-9P 618061-84-0P**
618061-85-1P 618061-86-2P 618061-87-3P
618061-88-4P 618061-89-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoquinazolines as inhibitors of epidermal growth factor receptor (EGF-R))

RN 618061-81-7 HCAPLUS

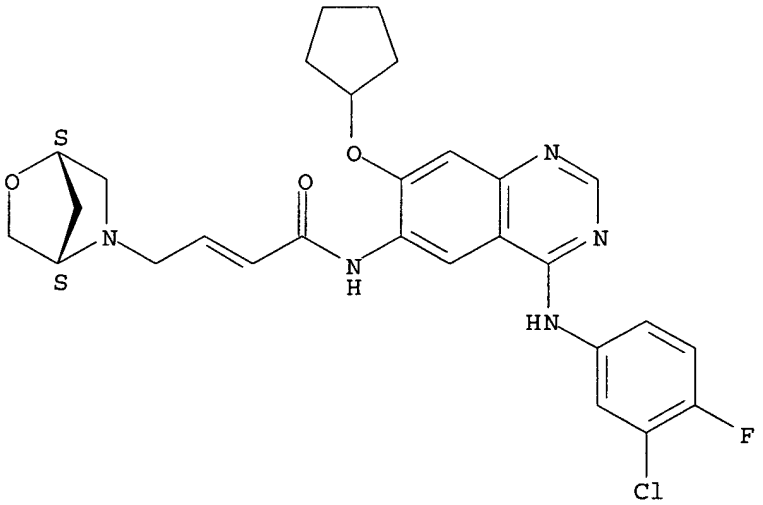
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



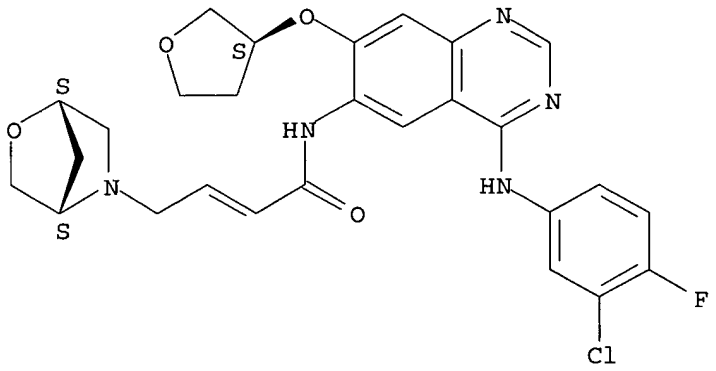
RN 618061-83-9 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



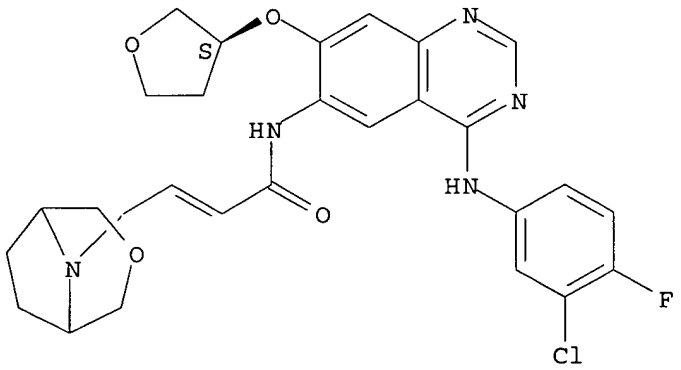
RN 618061-84-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



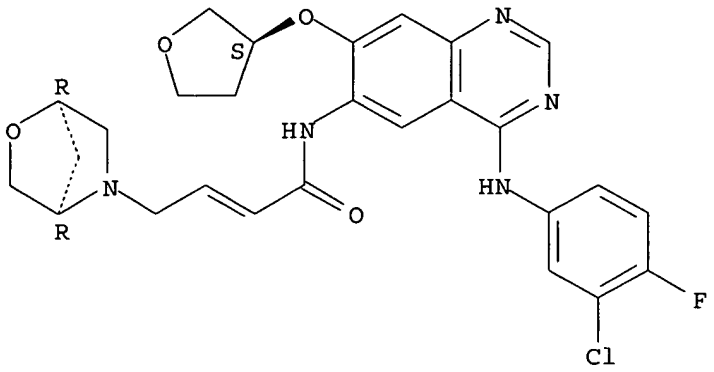
RN 618061-85-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



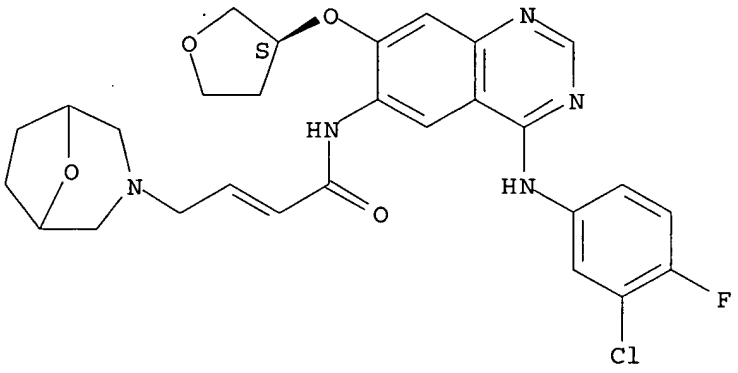
RN 618061-86-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(1R,4R)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



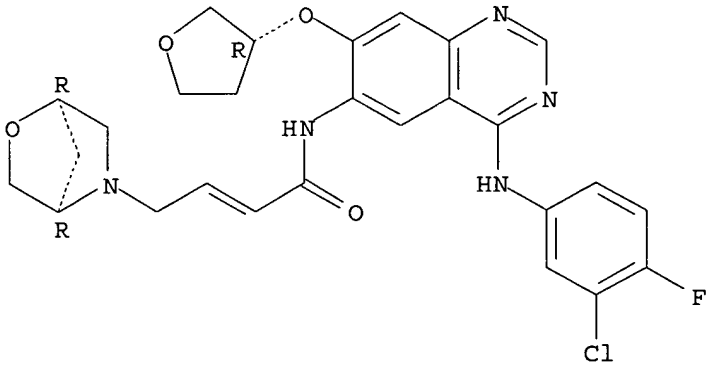
RN 618061-87-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



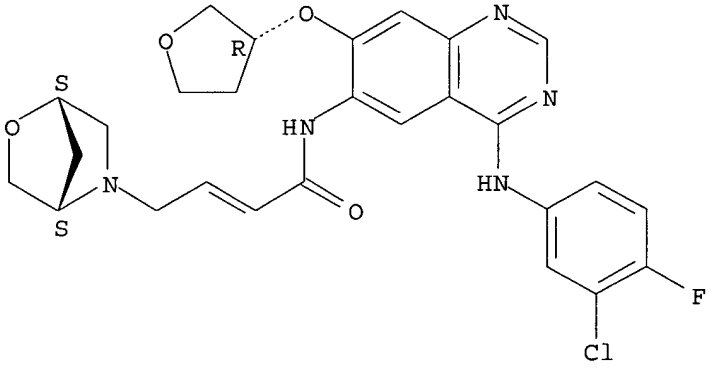
RN 618061-88-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(1R,4R)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 618061-89-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(1S,4S)-2-oxa-5-azabicyclo[2.2.1]hept-5-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:747043 HCAPLUS
DOCUMENT NUMBER: 135:303901
TITLE: Bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany
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FAMILY ACC. NUM. COUNT: 2
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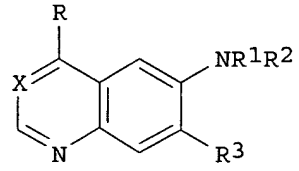
DE 10017539	A1	20011011	DE 2000-10017539	20000408

US 2001044435	A1	20011122	US 2001-816003		20010323
US 6627634	B2	20030930			
CA 2403152	AA	20011018	CA 2001-2403152		20010331
WO 2001077104	A1	20011018	WO 2001-EP3694		20010331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 2001063831	A5	20011023	AU 2001-63831		20010331
EP 1280798	A1	20030205	EP 2001-938076		20010331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003530395	T2	20031014	JP 2001-575577		20010331
PRIORITY APPLN. INFO.:			DE 2000-10017539	A	20000408
			DE 2000-10040525	A	20000818
			WO 2001-EP3694	W	20010331

OTHER SOURCE(S): MARPAT 135:303901

GI



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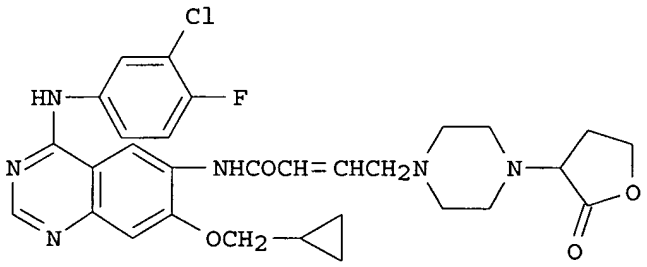


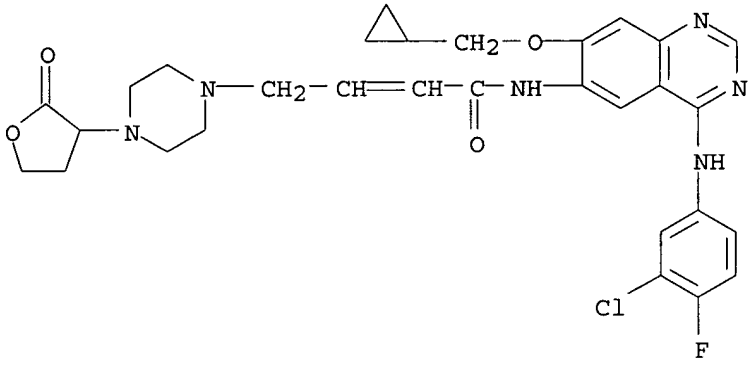
II

AB Bicyclic heterocycles I [X = N, CCN; R = substituted NH2; R1 = H, alkyl; R2 = acyl; R3 = H, (un)substituted alkoxy, cycloalkoxy, tetrahydrofuranyloxy, tetrahydropyranyloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy] were prepared for use as inhibitors of tyrosine kinase-mediated signal transduction for treatment of tumors and diseases of the lung and airway. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-7-fluoro-6-nitroquinazoline was treated with cyclopropylmethanol, followed by reduction to the amine, reaction with 4-bromocrotonic acid and N-tert.-butoxycarbonylpiperazine, and deblocking to give the quinazoline II. II had an IC50 for inhibition of epidermal growth factor dependent proliferation of 0.05 nM.

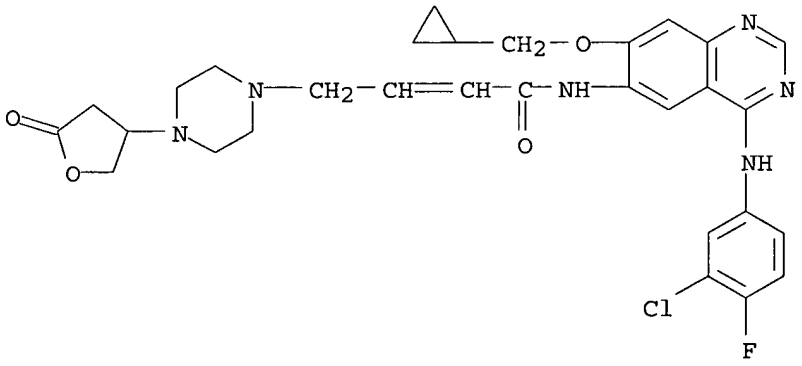
IT **365532-35-0P 365532-39-4P 365532-42-9P 365532-45-2P 365532-47-4P 365532-48-5P 365532-49-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

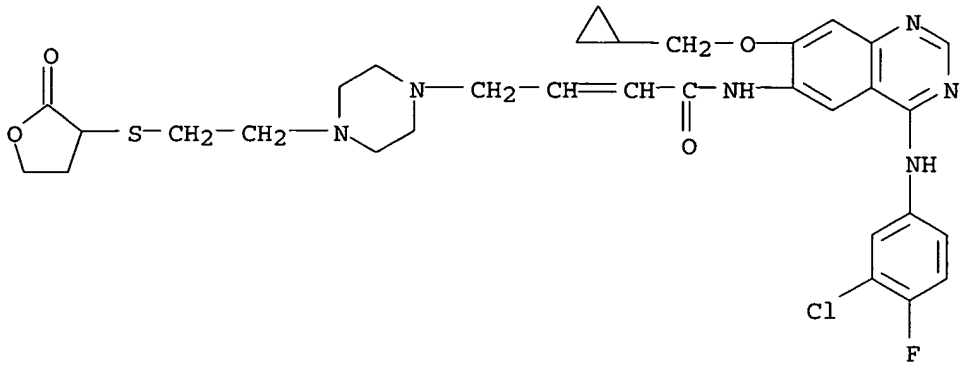
RN 365532-35-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



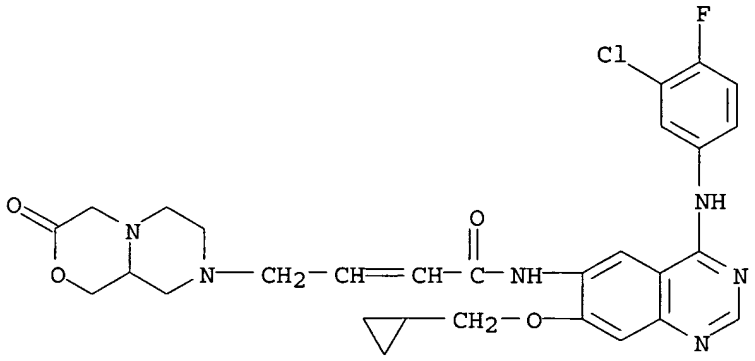
RN 365532-39-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-5-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



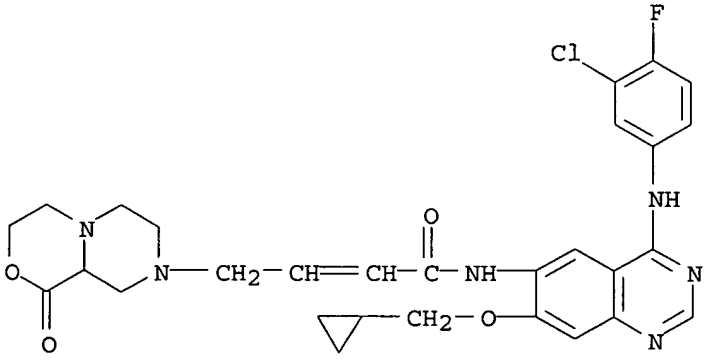
RN 365532-42-9 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[2-[(tetrahydro-2-oxo-3-furanyl)thio]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 365532-45-2 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-3-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)

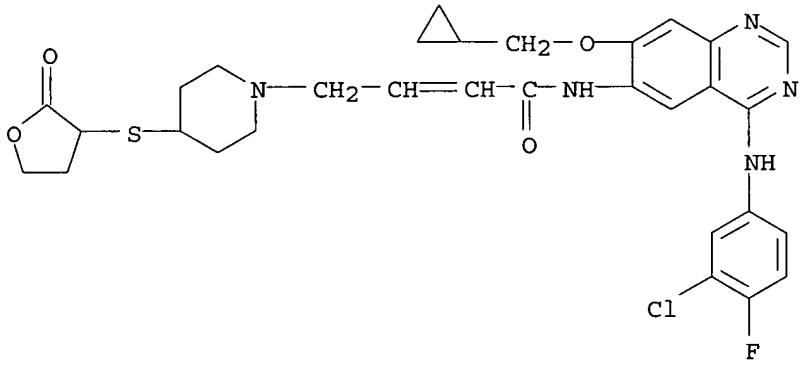


RN 365532-47-4 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-1-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)

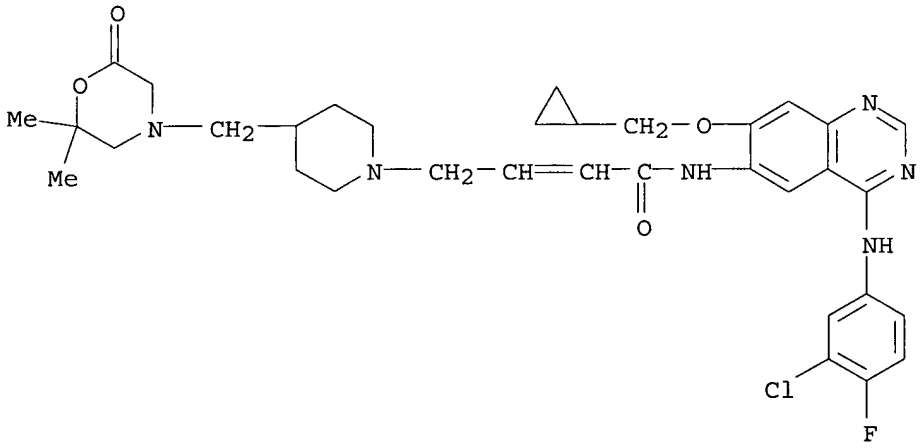


RN 365532-48-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-

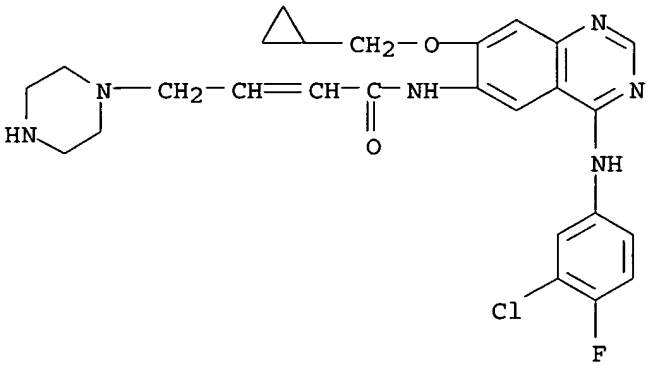
6-quinazolinyl]-4-[4-[(tetrahydro-2-oxo-3-furanyl)thio]-1-piperidinyl]-
(9CI) (CA INDEX NAME)



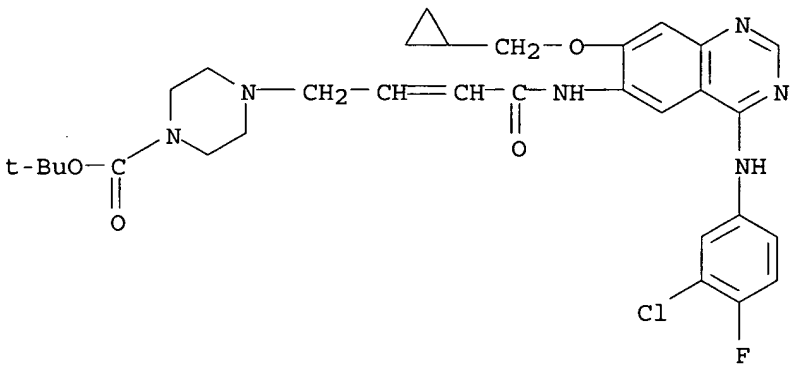
RN 365532-49-6 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)



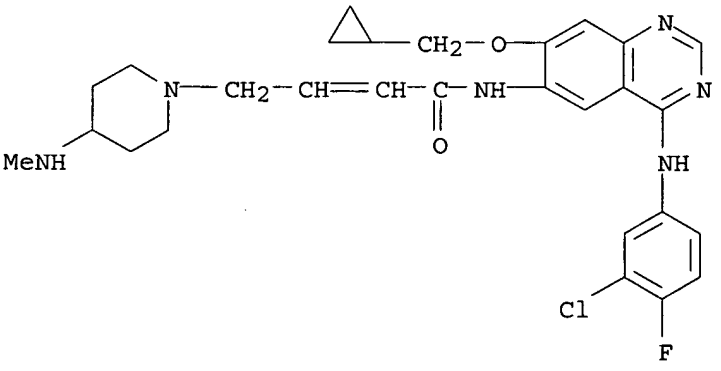
IT **290303-47-8P 290304-01-7P 365532-06-5P**
365532-18-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)
RN 290303-47-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 290304-01-7 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

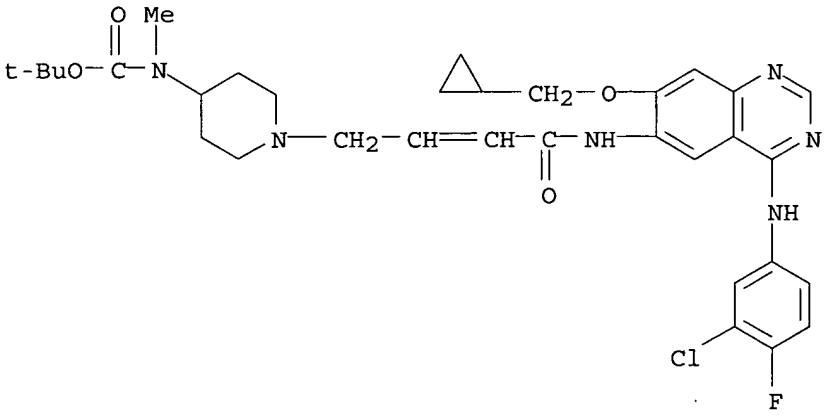


RN 365532-06-5 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(methylamino)-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 365532-18-9 HCAPLUS
CN Carbamic acid, [1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-

piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

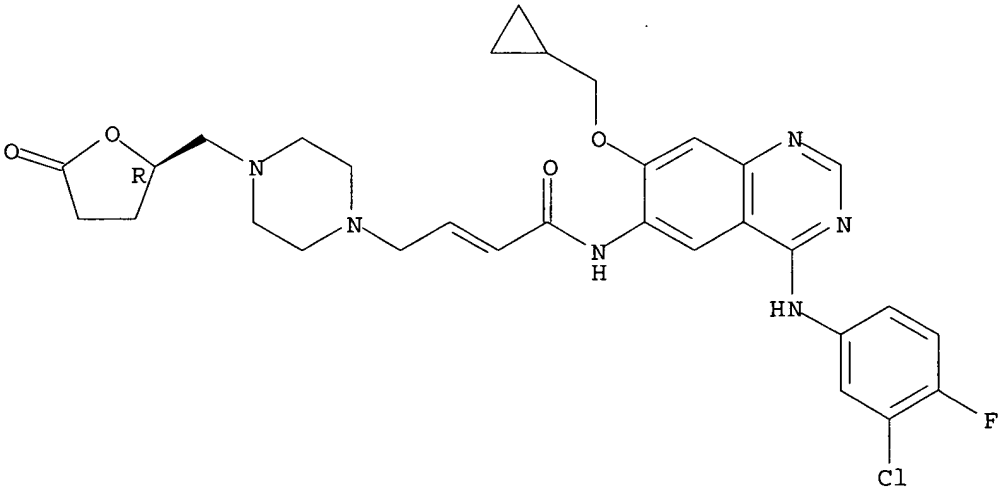


IT **365532-36-1P 365532-37-2P 365532-41-8P**
365532-43-0P 365532-44-1P 365532-46-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

RN 365532-36-1 HCAPLUS

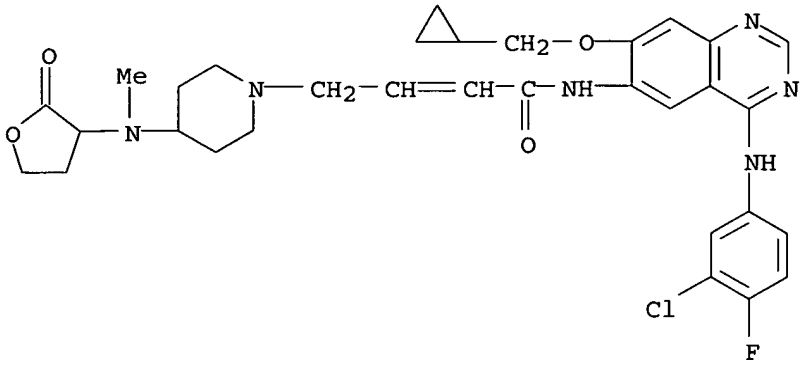
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[[(2R)-tetrahydro-5-oxo-2-furanyl]methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



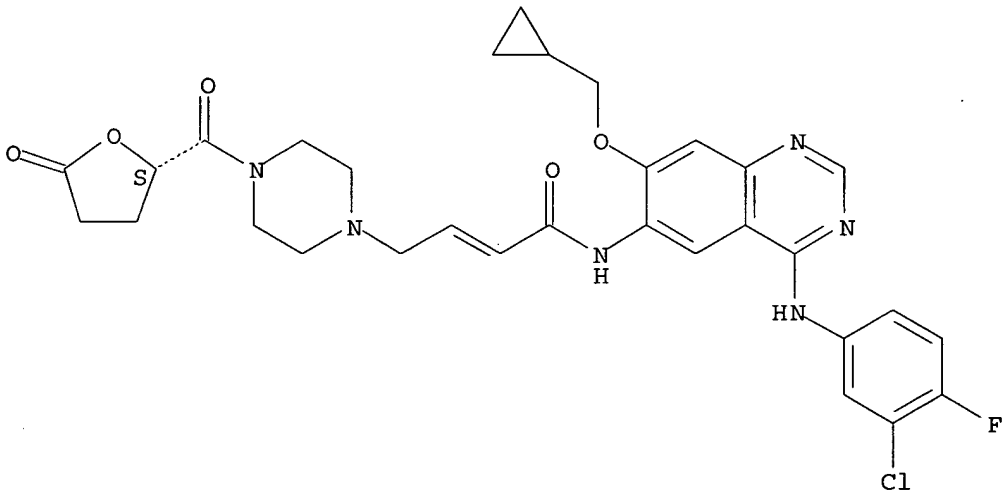
RN 365532-37-2 HCAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

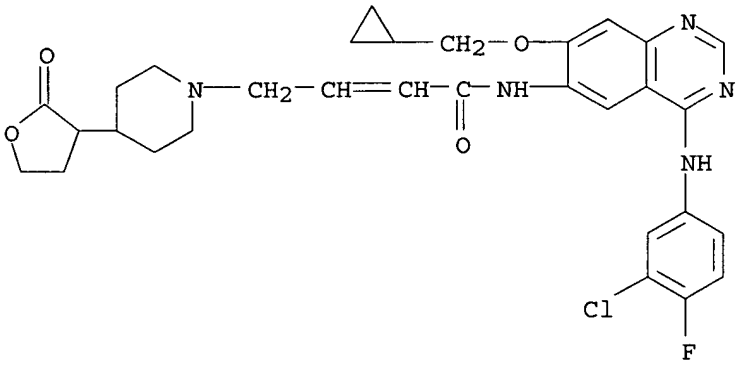


RN 365532-41-8 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

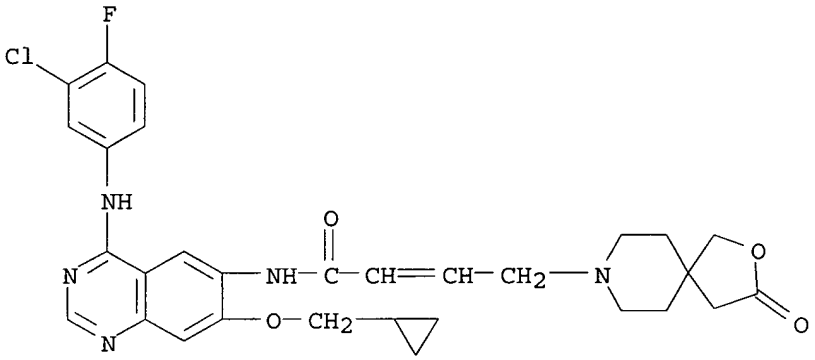
Absolute stereochemistry.
Double bond geometry unknown.



RN 365532-43-0 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 365532-44-1 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(3-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)



RN 365532-46-3 HCAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)